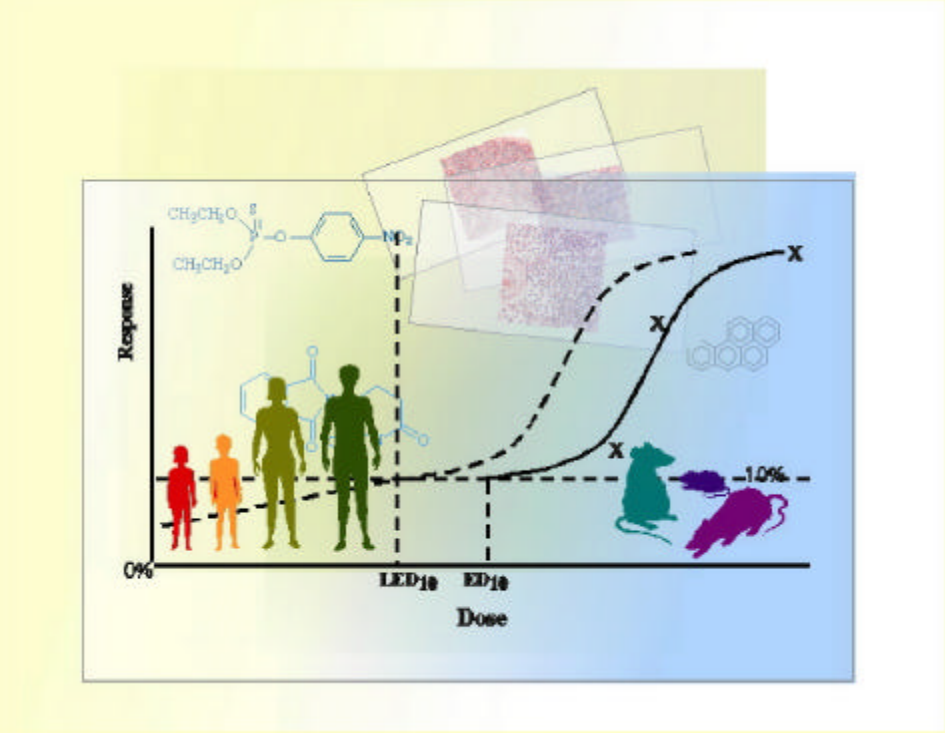
# HUMAN HEALTH RISK ASSESSMENT

# METHAMIDOPHOS




U.S. Environmental Protection Agency
Office of Pesticide Programs
Health Effects Division (7509C)

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# HUMAN HEALTH RISK ASSESSMENT

# METHAMIDOPHOS

## Phase 4

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**METHAMIDOPHOS REVISED RISK ASSESSMENT**
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# 1 Executive Summary

The Health Effects Division (HED) has conducted a human health risk assessment for the active ingredient **methamidophos** (O,S-dimethyl phosphoramidothioate) for the purpose of making a reregistration eligibility decision.

Methamidophos (O,S-dimethyl phosphoramidothioate) is a restricted use pesticide that is used as an insecticide in agricultural settings. It should also be noted that methamidophos is one of 22 chemicals on the United Nations list of chemicals requiring prior informed consent (PIC) procedures. On this list methamidophos is a PCU (problems under conditions of use), which are pesticides which are not banned or restricted in developed (industrialized) countries, but which have been shown to cause problems when used without the sophisticated application technologies required to mitigate risks. Methamidophos is formulated as a liquid product containing 40 percent active ingredient and is known as Monitor 4. As a result of an agreement between the registrant of methamidophos and EPA, methamidophos currently may be applied only to potatoes, tomatoes, and cotton. All uses other than potatoes and cotton have been deleted from the FIFRA Section 3 labels as of December 31, 1997. Under the same agreement, the use patterns for tomatoes are limited to those on FIFRA Section 24 (c) labels in 11 States. Recently, the registrants have announced their intention to support use of methamidophos products on three imported commodities, peppers, strawberries, and squash (PP#9E5040). There is an existing tolerance for methamidophos on peppers, but none has been established for the latter two commodities. The dietary risk assessment included these proposed uses.

HED evaluated the toxicology, residue chemistry, and occupational exposure databases for methamidophos and determined that the data are adequate to support a reregistration eligibility decision. This is an unusual assessment because methamidophos is a metabolite of another registered pesticide, acephate. Consequently, this assessment will encompass the risk of methamidophos from applications of acephate and of methamidophos. Acute and chronic dietary risk assessments were conducted as was a qualitative assessment of the potential exposure to methamidophos through drinking water. An aggregate risk assessment which determines the risk from methamidophos from both acephate and methamidophos application was also conducted. Since methamidophos is not used in a residential setting, an assessment of residential exposure was not conducted. As a result, the quantitative assessment of aggregate risk includes only dietary exposure. There are residential uses of acephate. For informational purposes, potential methamidophos exposure from residential uses of acephate have been included in this human health assessment as well as the acephate human health assessment. HED also considered dermal and inhalation exposure to occupational handlers as well as to workers reentering the treated fields.

Methamidophos is an organophosphate. As with other chemicals in its class, cholinesterase inhibition is the major toxic effect of methamidophos; however, other toxic effects were observed in the toxicology studies.

Methamidophos is acutely toxic, causing death shortly after exposure to relatively low oral, dermal, or inhalation doses. Methamidophos is only moderately irritating to the eyes and only mildly irritating to the skin. However, deaths and other signs of systemic toxicity occurred shortly after dermal or ocular application. These findings suggest that methamidophos is rapidly absorbed via these routes. Other toxic signs observed in animals treated acutely with methamidophos are consistent with cholinesterase inhibition (ChE) and are typical of the acute toxic signs induced by the organophosphates. They included: tremors, salivation, chromodacryorrhea (bloody tears) and dyspnea (labored breathing). There is no indication of carcinogenicity. The details of the toxicological data are presented in the Toxicology Chapter of the RED (Attachment 1).

Toxicity endpoints were selected based on cholinesterase (ChE) inhibition of the red blood cell, brain and plasma. The specific doses and endpoints selected by the HED Hazard Identification Assessment Review Committee ( see HED Document Nos. 012477 and 012921) for risk assessment were:

- ❏ Acute dietary - NOAEL = 0.3 mg/kg/day based on brain cholinesterase inhibition in an acute neurotoxcity study in rats at 0.7 mg/kg/day.

- ❏ Chronic dietary - NOAEL = 0.03 mg/kg/day based on plasma, erythrocyte and brain cholinesterase inhibition at 0.06 mg/kg/day from a 8 week toxicity study on rats.

- ❏ Short-term and intermediate-term dermal - NOAEL = 0.75 mg/kg/day based on brain cholinesterase inhibition at 11.2 mg/kg/day from a 21-day dermal study on rat.

- ❏ Short-term and intermediate-term inhalation - NOAEL = 0.001 mg/L based on a plasma, brain and erythrocyte cholinesterase inhibition at 0.005 mg/L from a 90 day inhalation study in rats.

All doses for risk assessment purposes were assessed the conventional safety factors of 10x for interspecies extrapolation and 10x for intraspecies variability. In addition, HED's FQPA Safety Factor Committee (FQPA SFC) considered the increased susceptibility of infants and children to methamidophos (8/ /98). Based on the developmental and reproductive toxicity studies reviewed, there does not appear to be any special sensitivity for pre- or post-natal effects; however, there is an indication of neurotoxic effects in hens and in humans. HED has therefore determined that for methamidophos the 10-fold uncertainty factor for the protection of infants and children as required under FQPA would be reduced to 3X. A developmental neurotoxicity study is needed to properly evaluate the neurotoxicity of this chemical.

A reference dose (RfD) which includes the FQPA safety factor (3X) is defined as the Population Adjusted Dose (PAD). In the case of methamidophos, the acute and chronic PADs include the FQPA safety factor of 3x and are therefore equivalent to the acute and chronic RfDs/3, respectively.

The methamidophos dietary risk assessments reflect highly refined exposure assessments; the anticipated residues and percent crop treated information were incorporated. Refinements were conducted in anticipation of a cumulative risk assessment being conducted in the future and also permit a more realistic comparison of Drinking Water Levels of Comparison (DWLOC) with estimates of potential drinking water concentrations provided by the Environmental Fate and Effects Division (EFED). A probabilistic/Monte Carlo acute dietary assessment was conducted using an acute population adjusted dose (aPAD) of 0.001 mg/kg/day; acute risk from application of methamidophos only resulted in 55% of aPAD consumed for the general U.S. population and 72% of the aPAD consumed for children (1 to 6 years old), the most highly exposed subpopulation**.** Chronic risks calculated using a chronic PAD (cPAD) of 0.0001 mg/kg/day were low. Chronic dietary risk resulted in 7% and 15% of the cPAD consumed for the general U.S. population and children(1 to 6 years old, again the most highly exposed subgroup), respectively.

In examining aggregate exposure, FQPA directs EPA to take into account available information concerning exposures from pesticide residues in food and other exposures for which there is reliable information. These other exposures include drinking water and non-occupational exposures, e.g., to pesticides used in and around the home. Risk assessments for aggregate exposure consider both short-, intermediate- and long-term (chronic) exposure scenarios considering the toxic effects which would likely be seen for each exposure duration.

There are no residential uses of methamidophos; therefore, the considerations for aggregate exposure are those from food and water. Additionally, since methamidophos is a metabolite of acephate, aggregate risk assessments which determine the methamidophos risks from application of both acephate and methamidophos, and from applications of methamidophos alone were conducted. For chronic aggregate risk (food only), chronic exposures to methamidophos from application of acephate and application of methamidophos were combined and compared to the methamidophos reference dose. This assessment was conducted using anticipated residues and BEAD % crop treated information. Results of the chronic exposure analysis show that 23% of the cPAD is consumed for the U.S. population. The most significantly exposed subpopulation, children (1 to 6 years ) occupied 37% of the cPAD, respectively. The results indicate that HED has no concern for chronic aggregate exposure from food alone.

An acute aggregate dietary exposure analysis (food only) which considers methamidophos from application of acephate and of methamidophos was also conducted. Residue refinements including anticipated residues generated from field trial and monitoring data, adjustments for percent crop treated, washing and cooking

factors and a probabilistic/Monte Carlo acute analysis were utilized. Applying all of these refinements, the most highly exposed population subgroup was children 1-6 years with a %aPAD of 120%. For the general U.S. population, 79% of the aPAD was consumed. The results indicate that for children, 100% of the aPAD is exceeded.

Conservative Tier II (PRZM-EXAMS) modeling was provided by EFED and indicate that methamidophos concentrations in surface water are not likely to exceed 48 ppb for peak (acute ) exposure and 0.9 ppb for mean (chronic) exposure. The lack of acceptable aerobic aquatic metabolism data increased the uncertainty of the chronic EEC's. Methamidophos is not expected to leach to groundwater because methamidophos is not persistent under aerobic conditions. Consequently, using the SCI-GROW model to estimate concentrations of methamidophos in ground water, resulted in low EECs for both acute and chronic exposure at 0.028 ug/L. If any methamidophos residues reached ground water, it is expected to persist.

Using these conservative water models, estimated water concentrations of methamidophos do not exceed the chronic Drinking Water Levels Of Comparison (DWLOCs) but do exceed the acute DWLOCs for surface water only. Consequently, there may be some concern for methamidophos in drinking water. Drinking water monitoring data would allow refinement of the estimated environmental concentrations (EECs).

An aggregate exposure assessment which considers risk from food (from application of acephate and application of methamidophos) and water was conducted for chronic exposure only since HED has concerns for acute aggregate exposure from food alone and because DWLOCs calculated for acute exposure from the application of methamidophos alone indicate that methamidophos residues in surface water may be of concern. Using the aggregate chronic food exposure (exposure which incorporates methamidophos residues from application of both methamidophos and acephate), DWLOCs were calculated (Table 7). The results indicate that there may be concern for children(1 to 6 years) and infants.

The occupational assessment was completed using the maximum use rate of 1 lb ai/acre (lb ai/A). HED assesses potential exposure to pesticides at the maximum label rate for all pesticides to assure adequate protection for all workers. The anticipated use patterns and current labeling indicate 5 major occupational handler exposure scenarios based on the types of equipment and techniques that can be used to make methamidophos applications. These 5 scenarios serve as the basis for the quantitative risk assessment developed for occupational handlers. The 5 scenarios are: (1a) mixing/loading of liquid formulation for aerial application and chemigation (potatoes only); (1b) mixing/loading of liquid formulation for ground boom application; (2) applying sprays with a fixed-wing aircraft; (3) applying sprays with a helicopter, (4) applying sprays with groundboom equipment and (5) flagging aerial spray applications. The 5 scenarios were evaluated considering 3 levels of protection for the worker. The levels include: baseline clothing (long sleeved shirt and long pants), PPE (personal protective equipment, baseline clothing under coveralls, chemical resistant gloves, and

a dust/mist respirator), and engineering controls (closed system mixing and loading and enclosed cab on tractor or aircraft). Short- and intermediate-term dermal and inhalation margins of exposure (MOEs) were combined for each scenario and each level of protection.

Each occupational handler exposure scenario was evaluated using the Pesticide Handlers Exposure Database (PHED) Version 1.1 (August 1998) since HED has not received any chemical-specific occupational exposure studies for methamidophos. Submission of chemical-specific exposure studies could refine the risk calculations.

HED has concerns for occupational handlers of methamidophos. Risks were below the Agency's level for concern (MOE >100) for only two scenarios, each considered with engineering controls (the highest level of occupational risk mitigation). These scenarios were (4) applying sprays with groundboom with engineering controls (enclosed cab) and (5) flagging for aerial application with engineering control(flagger inside a closed vehicle). The combined MOEs for the remaining scenarios at the different levels of protection ranged as follows: Baseline clothing (0.052 to 41); PPE ( 8 to 58); and Engineering Control (17 to 630).

Postapplication exposure assessment of methamidophos use on tomatoes, potatoes and cotton was calculated based on review of the three submitted DFR studies on tomatoes and potatoes. The tomato data served as surrogate dissipation rate for cotton, whether this over- or under- estimated the dissipation rate is uncertain. From these studies it appears that the restricted entry intervals (REIs) will have to be increased to protect workers. The current REIs listed on labels are Worker Protection Standard (WPS) default values assigned in lieu of empirical data. For the current REIs of 48 to 72 hrs, the MOEs range between 4 and 20. Based on chemical specific data, acceptable MOEs were not achieved until 8 - 31 days post-treatment, depending on the scenario.

Although there are no residential uses of methamidophos *per se*, the public may be exposed to methamidophos upon entering residential areas which have been previously treated with acephate. The available data indicated that residential acephate uses result in potential short-term dermal and oral acephate and methamidophos post-application residential exposures to the public. However, post-application inhalation exposures are not anticipated as a result of residential use of acephate.

It is anticipated that adults and children may primarily be exposed to acephate and methamidophos through their contact with acephate-treated turfgrass and soil. The analyses indicated that none of the acephate post-application residential exposure scenarios result in methamidophos exposures that exceed HED's level of concern (MOE range = 820 - 600,000). It should be noted that the residential SOPs specify that the residential exposure calculations are to be used on a screening basis.

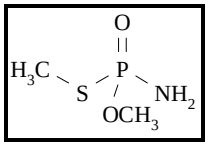
The public may also be exposed to acephate and methamidophos upon entering recreational areas (golf courses) which have been previously treated with acephate.

The possible post-application exposures are short-term dermal exposures; inhalation exposure is not expected. The recreational areas addressed in this assessment are golf courses.

The results indicated that MOEs for adult golfers' risks to methamidophos were 125,000 while the calculated MOEs for 13+ year-old golfers' risks to methamidophos were 78,100.

## 2 Physical/Chemical Properties Characterization

Methamidophos



Empirical Formula: $C_2H_8NO_2PS$
Molecular Weight: 141.1
CAS Registry No.: 10265-92-6
Shaughnessy No.: 101201

Methamidophos is a colorless to white crystalline solid with a strong mercaptan-like odor and a melting point of 46.1 °C. Methamidophos is readily soluble (>200 g/L) in water, acetone, dimethylformamide, dichloromethane, and 2-propanol, and is soluble in n-octanol at 50-100 g/L, toluene at 2-5 g/L, and n-hexane at <1 g/L.

Three methamidophos manufacturing-use products (MPs) are registered under Shaughnessy No. 101201: the Bayer Corporation 72% technical product and 60% formulation intermediate (T and FI; EPA Reg. Nos. 3125-341 and 3125-348, respectively), and the Valent U.S.A. Corporation 72% T (EPA Reg. No. 59639-68). We note that the Valent 72% T was transferred from Chevron (EPA Reg. No. 62499-21; 10/4/91). Only the registered 72% Ts and 60% FI are subject to a reregistration eligibility decision.

## 3 Hazard Characterization

Although a developmental neurotoxicity study was identified as a data gap by the HED Hazard Identification Assessment Review Committee (HIARC), the toxicology database for methamidophos is adequate to assess its toxicity and permits a reregistration eligibility decision to be made. Tables 1 and 2 present the acute toxicity profile for methamidophos and the HIARC toxicity endpoints and doses for risk assessment, respectively.

### 3.1 Hazard Profile

Methamidophos is acutely toxic (Toxicity Category I), causing death shortly after exposure to relatively low oral, dermal, or inhalation doses. Methamidophos is only moderately irritating to the eyes and only mildly irritating to the skin. However, deaths and other signs of systemic toxicity occurred shortly after dermal or ocular application. These findings suggest that methamidophos is rapidly absorbed via these routes. Other toxic signs observed in animals treated acutely with methamidophos are consistent with cholinesterase (ChE) inhibition and are typical of the acute toxic signs induced by the organophosphates. They included tremors, salivation, chromodacryorrhea (bloody tears) and dyspnea (labored breathing).

Sufficient data are available on the subchronic toxicity of methamidophos. The most consistent toxicological findings associated with exposure to methamidophos were decreased body weight gain (rats) and inhibition of plasma, erythrocyte and/or brain cholinesterase (hens, rats, dogs and humans). Regardless of the route of exposure (oral, dermal or inhalation), cholinesterase inhibition was consistently detected from the initial sampling time (generally 1 week) to study termination. In general, the magnitude of the response did not increase significantly with time after week 1.

A subchronic oral human study was submitted and evaluated (MRID No. 00015160). The study is considered unacceptable based on the absence of raw data (i) to support conclusions regarding various clinical measurements; (ii) the dosing schedule of individuals; and (iii) the method used to assign individuals to various treatment groups. Also the method used for cholinesterase measurements was not reported.

In addition to these deficiencies, the unsupervised weekend dosings, lack of records of food intake and insufficient number of subjects per test group constituted weak points in the study.

Furthermore, OPP continues to state its policy to make no final decisions under FQPA relying on toxicity studies with human subjects until a robust policy is in place including ethical and scientific standards for their acceptability. In the absence of such a policy, and of the report of the SAB/SAP subcommittee who met in December 1998, the ethical acceptability of old or new human studies has not been assessed.

Sufficient data are available to assess the chronic toxicity and carcinogenic potential of methamidophos. In agreement with the data from subchronic studies, the most consistent toxicological findings following chronic methamidophos exposure were decreased body weight gain (rats and mice) and inhibition of plasma, erythrocyte and/or brain cholinesterase (rats and dogs). In addition, methamidophos has been classified in **"Group E"** (i.e., the chemical is characterized as **"Not Likely"** to be carcinogenic in humans via relevant routes of exposure) because there is no evidence that methamidophos altered the spontaneous tumor profile in rats or mice.

Four developmental toxicity studies (two with rats and two with rabbits) and two reproductive toxicity studies were available for review. These data are considered adequate to assess the developmental and reproductive toxicity potential of methamidophos. There is no indication of an increased sensitivity of the offspring of rats or rabbits to pre-natal or postnatal exposure to methamidophos. In all studies examined, maternal or parental NOAELs are lower or equivalent to the offspring NOAELs. Nevertheless, a weight-of-the-evidence evaluation of the database indicates the need for evaluation of functional developmental parameters and thus a need to conduct a developmental neurotoxicity study.

Available mutagenicity studies (MRID No. 00098457, 4285470, 42854701, 41461401, 41461401, 41234306, 41234306, 41234305 and 41234305) indicate that methamidophos is not mutagenic in bacteria but does induce gene mutations in cultured mammalian cells at high S9-activated levels. There was evidence of clastogenicity at high nonactivated concentrations and polyploidy at high S9-activated doses. In contrast, methamidophos was negative for chromosome aberrations in vivo and did not induce UDS in vitro. The data suggest, therefore, that the marginal genotoxicity activity seen with the test substance is not expressed in vivo. The lack of an oncogenic effect in the rat or mouse long-term feeding studies and the absence of significant reproductive or developmental toxicity that could be associated with a mutagenic mode of action (i.e., germ cell damage, reduced numbers of pregnancies, decreased total implants, increased resorptions) support this conclusion. Based on these considerations, HED concludes that there is no concern for mutagenicity.

In a metabolism study (MRID No. 00015224) with oral dosing, methamidophos was absorbed and rapidly degraded and/or eliminated within the first 24 hours postdosing. In the $^{14}C$ studies, 60% of the radioactivity was detected in $CO_2$ and 11% in urine. Fecal excretion of radiolabel was low. In the $^{32}P$ studies, $\approx$70% of the radioactivity was detected in the urine. Fecal excretion of the $^{32}P$ radiolabel was initially low (2-3%) but increased 3-21 days postdosing (8-21%). The identified metabolites in the urine (O,S-dimethyl-phosphorothioate, methyl dihydrogen phosphate and phosphoric acid) are not expected to be significant ChE inhibitors. Residues of methamidophos in tissue 14 days posttreatment were $<$0.004 ppm. There was no difference in the rate of metabolism, excretion or nature of the metabolites between males and females.

Acceptable acute and subchronic delayed neurotoxicity studies in hens and

acute and subchronic neurotoxicity screening batteries in rats were available for review. There were no data gaps for the assessment of the neurotoxic potential of methamidophos. Data from the hen studies indicate that methamidophos produces toxic signs characteristic of ChE inhibition (acute and subchronic exposures), inhibition of ChE and neurotoxic esterase (NTE) activity in brain and spinal cord (subchronic exposure) but no delayed neurotoxicity (except at high doses as discussed below) or histological changes in brain, spinal cord or peripheral nerves. In rats, methamidophos induced neurobehavioral effects e.g., reduced motor and locomotor activities, tremors and decreased forelimb grip, and ChE inhibition following both acute and subchronic exposure. There were, however, no treatment-related gross or histopathological effects and brain weights were unaffected by treatment. Neurobehavioral effects in both the acute and subchronic studies occurred at doses that were only slight higher than the lowest dose at which ChE inhibition was detected. Special studies conducted with methamidophos (racemate and enantiomers) showed evidence of delayed neurotoxicity in hens following ingestion of high doses (12-16x the oral $LD_{50}$). Similarly, information in the open literature indicated that methamidophos can cause delayed neurotoxicity in humans following exposure to excessive, life threatening concentrations.

**Table 1A. Acute Toxicity**

| Guideline No. | Study Type | MRIDs # | Results | Tox Cat. | Core Grade |
|---|---|---|---|---|---|
| **Acute Toxicity** | | | | | |
| 81-1 | Acute Oral; Rat 95.0% a.i. | 00014044 | $LD_{50}$ = 15.6 mg/kg ♂<br>$LD_{50}$ = 13.0 mg/kg ♀ | I | Acceptable |
| 81-2 | Acute Dermal; Rabbit 75% a.i. | 00014049 | $LD_{50}$ = 118 mg/kg ♂ | I | Acceptable |
| 81-3 | Acute Inhalation; Rat 70.5% a.i. | 00148449 | $LC_{50}$ = 0.052-0.079 mg/L[a] ♂<br>$LC_{50}$ = 0.062-0.128 mg/L[a] ♀ | I | Acceptable |
| 81-4 | Primary Eye Irritation; Rabbit 72.3% a.i.; dose: 0.1 mL | 00014221 | Corneal opacity and pannus present in 2/6 rabbits for 10 days posttreatment. One death 30 min. after dosing | I | Acceptable |
| 81-5 | Primary Skin Irritation; Rabbit 73% a.i. dose: 0.1 mL | 00014220 | PIS = 0.6 but test material was lethal to 5/9 animals within 24 hrs. of treatment | I | Acceptable |
| 81-6 | Dermal Sensitization; Guinea Pig 73.8% a.i. | 00147929 | Not a skin sensitizer (modified Buehler test) | -- | Acceptable |

**Table 1B. Toxicity Profile of Methamidophos**

| Guideline No. | Study Type | MRIDs # | Results | Effects | Core Grade |
|---|---|---|---|---|---|
| **Subchronic Toxicity** | | | | | |
| **82-1(a) 870.3100** | 90-day feeding-rat | 0014155 | NOAEL = 1.0 mg/kg/day<br>LOAEL = 3 mg/kg/day<br><br>ChE NOAEL = 0.1 mg/k/day<br>ChE LOAEL = 0.3 mg/kg/day | Decreased male body weight gain and decreased food consumption and clinical signs in both sexes<br><br>Plasma and RBC ChE inhibition in both sexes | Acceptable |
| **82-1(a) 870.3100** | 90-day feeding-dog | 00014153 | NOAEL = 0.375 mg/kg/day<br>LOAEL = not determined<br><br>ChE NOAEL = 0.0375 mg/k/day<br>ChE LOAEL = 0.125 mg/kg/day | No effect on appearance, behavior, mortality, food intake, body weight, hematology, clinical chemistry, urinalysis, organ weight or gross necropsy<br><br>Plasma and RBC ChE inhibition in both sexes | Acceptable |
| **82-2 870.3200** | 21-day dermal-rat | 44525301 and 44525301 | NOEL =0.749 mg/kg/day<br>LOEL =11.2 mg/kg/day | Brain, RBC and plasma cholinesterase inhibition | Acceptable |
| **82-3 870.3465** | 90- day subchronic inhalation- rats | 41402401 | NOEL= 0.005 mg/L<br>LOEL =0.0231 mg/L<br><br>ChE NOAEL = 0.001 mg/L<br>ChE LOAEL = 0.005 mg/L | Clinical signs, decreased body weight gain and feed consumption, altered clinical chemistry parameters, and decreased spleen weights<br><br>Brain, RBC and plasma cholinesterase inhibition | Acceptable |
| **82-1 special ChE study** | subchronic oral - rat | 41867201 | NOEL= 0.03 mg/kg/day<br>LOEL =0.06 mg/kg/day | Brain, RBC and plasma cholinesterase inhibition | Acceptable |

| Guideline No. | Study Type | MRIDs # | Results | Effects | Core Grade |
|---|---|---|---|---|---|
| **82-1** | subchronic oral -human | 00015160 | 1:4 mixture:<br>NOAEL (both sexes) = 0.1 mg/kg/day (≈0.02 mg/kg methamidophos);<br>LOAEL = 0.2 mg/kg/day (≈0.04 mg/kg methamidophos)<br><br>1:9 mixture:<br>NOAEL (♂) = 0.2 mg/kg/day (≈0.02 mg/kg methamidophos);<br>LOAEL = 0.3 mg/kg/day (≈0.03 mg/kg methamidophos)<br><br>1:9 mixture:<br>NOAEL (♀) = 0.3 mg/kg/day (≈0.03 mg/kg methamidophos);<br>LOAEL = 0.4 mg/kg/day (≈0.04 mg/kg methamidophos) | Plasma cholinesterase inhibition | Un-acceptable |
| **Chronic Toxicity** | | | | | |
| 83-1(b) 870.4100 | 1-year chronic oral- dog | 00147938 and 41234304 | NOEL=**>**0.8 mg/kg/day<br>LOEL =not established<br><br>ChE NOAEL = not established<br>ChE LOAEL ≈0.05 mg/kg/day | No significant effects on mortality, clinical signs, body weights, food consumption, hematology, clinical chemistry, urinalysis, organ weights, or gross and histologic pathology<br><br>Brain, RBC and plasma cholinesterase inhibition | Acceptable |
| 83-2(b) 870.4200 | Carcinogenicity - mouse | 0014557, 00147937, and 43248101 | NOEL= 0.7 mg/kg/day<br>LOEL **=**3.6 mg/kg/day<br>oncogenic NOAEL = **>**3.6 mg/kg/day | Decreased body weight gain and feed consumption in males and females.<br><br>No treatment-related increases in tumor incidence when compared to controls. | Acceptable |

| Guideline No. | Study Type | MRIDs # | Results | Effects | Core Grade |
|---|---|---|---|---|---|
| **83-5 870.4300** | Combined chronic/Carcinogenicity -rat | 00148452 and 43248102 | NOEL=0.3 mg/kg/day<br>LOEL =0.9 mg/kg/day<br><br>ChE NOAEL = not established<br>ChE LOAEL= 0.1 mg/kg/day<br><br>oncogenic NOAEL =2.7 mg/kg/day | Decreased body weight gain in males<br><br>Brain, plasma and erythrocyte ChE inhibition<br><br>No treatment-related increases in tumor incidence when compared to controls. | Acceptable |
| **Developmental/Reproductive Toxicity** | | | | | |
| **83-3(a) 870.3700** | Developmental-Rat | 00148454 | Maternal<br>NOAEL = 1.0mg/kg/day<br>LOAEL = 3.0mg/kg/day<br><br>Developmental<br>NOAEL = 1.0mg/kg/day<br>LOAEL = 3.0mg/kg/day | Decreased body weight gain and feed consumption during pregnancy and signs indicative of cholinesterase inhibition (i.e., fasciculation, hyperactivity, salivation and lacrimation).<br><br>Decreased fetal weight | Acceptable |
| **83-3(a) 870.3700** | Developmental-Rat | 43906901 | Maternal<br>NOAEL = 0.14 mg/kg/day<br>LOAEL= 5.49 mg/kg/day<br><br>Developmental<br>NOAEL = 0.14 mg/kg/day<br>LOAEL = 5.49 mg/kg/day | Clinical signs (tremors, muscle fasciculations and salivation), decreased body weight gain and food consumption, and inhibition of ChE activities of plasma, RBC, and brain.<br><br>Decreased placental and fetal weights (males, females and combined); an increase in skeletal variations (incompletely ossified frontal bones, sacral arches and sternebrae [segments 3, 4] and xiphoid); and unossified metacarpals and sternebrae | Acceptable |
| **83-3(b) 870.3700** | Developmental-Rabbit | 00041315 | Maternal<br>NOAEL= not established<br>LOAEL = **<**0.1 mg/kg/day<br><br>Developmental<br>NOAEL= >2.5 mg/kg/day<br>LOAEL = not determined | Decreased body weight gain during gestation<br><br>No compound-related increases in fetal malformations or variations were seen. | Acceptable |

| Guideline No. | Study Type | MRIDs # | Results | Effects | Core Grade |
|---|---|---|---|---|---|
| **83-3(b) 870.3700** | Developmental-Rabbit | 44040601 | Maternal<br>NOAEL= 0.20 mg/kg/day<br>LOAEL = 0.65 mg/kg/day<br><br>Developmental<br>NOAEL= >2.47 mg/kg/day<br>LOAEL = not determined | Decreased body weight gain and decreased) food consumption<br><br>No effect on fetal development | Acceptable |
| **83-4 870.3800** | Two-generation Reproduction - Rat | 00148455 and 41234301 | Parental systemic<br>NOAEL = 0.5 mg/kg/day<br>LOAEL = 1.65 mg/kg/day<br><br>Reproductive<br>NOAEL = 0.5 mg/kg/day<br>LOAEL = 1.65 mg/kg/day<br><br>Developmental<br>NOAEL = 0.5 mg/kg/day | Decreased body weight of males and females during premating and of females during lactation.<br><br>Decreases in the number of sperm positive females giving birth.<br><br>Decreases in pup viability for the F1, F2a, and F2b generations and significant reductions in pup weight during lactation in the F1, F2a, and F2b generations. | Acceptable |
| **83-4 870.3800** | Two-generation Reproduction - Rat | 44466001, 44815401 and 44815402 | Parental systemic<br><br>LOAEL = 0.08 mg/kg/day (LDT)<br>NOAEL = <0.08 mg/kg/day<br><br>Offspring toxicity<br><br>LOAEL = 0.08 mg/kg/day (LDT)<br>NOAEL = <0.08 mg/kg/day | RBC and brain cholinesterase inhibition at the LDT<br><br>pup body weight decrements at the LDT | Acceptable |
| **Neurotoxicity** | | | | | |
| **81-7 870.6100** | Acute oral delayed neurotoxicity-hens | 00041217 | oral $LD_{50}$ = 29.75 mg/kg | N/A | Acceptable |

| Guideline No. | Study Type | MRIDs # | Results | Effects | Core Grade |
|---|---|---|---|---|---|
| **81-8ss 870.6200** | Acute neurotoxicity-rat | 43025001 | NOAEL =<0.9 mg/kg/day. LOAEL =0.9 mg/kg/day<br><br>ChE NOAEL = <0.9 mg/kg/day<br>ChE LOAEL = 0.9 mg/kg/day | slightly reduced motor/locomotor activity in males and females and clinical signs in one male consistent with neurotoxictiy secondary to ChE inhibition.<br><br>Serum, brain, and RBC ChE inhibition | Acceptable |
| **81-8ss 870.6200** | Acute neurotoxicity screening study in rats (Supplemental study) | 43345801 | The results of this study should be considered with those of another acute neurotoxicity study (MRID No. 43025001)<br><br>NOAEL = 0.7 mg/kg<br>LOAEL = 0.9 mg/kg,<br><br>ChE NOAEL = 0.3 mg/kg<br>ChE LOAEL = 0.7 mg/kg | no neurobehavioral effects<br><br>plasma, brain, and RBC ChE inhibition | Acceptable |
| **82–7 870-6200** | Subchronic neurotoxicity screening study in rats | 43197901 | Neurotoxicity<br>NOAEL = 0.067 mg/kg/day (males); 0.074 mg/kg/day for (females).<br>LOAEL =0.787 mg/kg/day (males) and 0.889 mg/kg/day (females).<br><br>ChE NOAELs<br>RBC: NOAEL = (0.067 mg/kg/day ♂; 0.074 mg/kg/day ♀)<br>LOAEL = 12 ppm (0.787 mg/kg/day ♂; 0.899 mg/kg/day ♀)<br><br>Plasma and brain = NOAEL = <1 ppm (<0.067 mg/kg/day ♂; <0.074 mg/kg/day ♀, lowest dose tested)<br>LOAEL = 1 ppm | reduced motor and locomotor activity, decreased body weight gain, and urine stains<br><br>plasma, brain, and RBC ChE inhibition | Acceptable |

| Guideline No. | Study Type | MRIDs # | Results | Effects | Core Grade |
|---|---|---|---|---|---|
| **82 -7 870.6200** | Subchronic oral delayed neurotoxicity-hens | 40985202 | NOAEL =0.3 mg/kg/day LOAEL =1 mg/kg/day | inhibition of plasma BuChE and spinal cord NTE activity. | Acceptable |

**Table 1C. Toxicity Profile - Mutagenicity & Metabolism**

| Guideline No. | Study Type | MRIDs # | Results | Core Grade |
|---|---|---|---|---|
| **84-2<br>870.5100<br>870.5375<br>870.5550** | Mutagencity studies | 00098457, 4285470, 42854701, 41461401, 41461401, 41234306, 41234306, 41234305 and 41234305 | The available studies indicate that methamidophos is not mutagenic in bacteria but does induce gene mutations in cultured mammalian cells at high S9-activated levels. Similarly, there was evidence of clastogenicity at high nonactivated concentrations and polyploidy at high S9-activated doses. In contrast, methamidophos was negative for chromosome aberrations *in vivo* and did not induce UDS *in vitro.* The data suggest, therefore, that the marginal genotoxicity activity seen with the test substance is not expressed *in vivo.* The lack of an oncogenic effect in the rat or mouse long-term feeding studies and the absence of significant reproductive or developmental toxicity that could be associated with a mutagenic mode of action (i.e., germ cell damage, reduced numbers of pregnancies, decreased total implants, increased resorptions) support this conclusion. Based on these considerations, HED concluded that there is no concern for mutagenicity. | Acceptable |
| **Metabolism** | | | | |
| **85-1<br>870.7485** | Metabolism | 00015224 | Methamidophos was absorbed and rapidly degraded and/or eliminated within the first 24 hours postdosing. In the $^{14}C$ studies, 60% of the radioactivity was detected in $CO_2$ and 11% in urine. Fecal excretion of radiolabel was low. In the $^{32}P$ studies, ≈70% of the radioactivity was detected in the urine. Fecal excretion of the $^{32}P$ radiolabel was initially low (2-3%) but increased 3-21 days postdosing (8-21%). The identified metabolites in the urine (O,S-dimethyl-phosphorothioate, methyl dihydrogen phosphate and phosphoric acid) are not expected to be significant ChE inhibitors. Residues of methamidophos in tissue 14 days posttreatment were <0.004 ppm. There was no difference in the rate of metabolism, excretion or nature of the metabolites between males and females. | Acceptable |

[a] 95% Confidence limit
NOAEL = No Observable Adverse Effect Level
LOAEL = Lowest Observable Adverse Effect Level
LDT = Lowest Dose Tested
ChE = Cholinesterase

### 3.2 Dose Response Assessment

The strengths and weaknesses of the methamidophos toxicology database were considered during the process of toxicity endpoint and dose selection. In general, all the required guideline studies on methamidophos were available and provided reasonable confidence when the toxicity endpoints and doses for risk assessment were selected. The HIARC recommended that a developmental neurotoxicity study be conducted for methamidophos because in studies from the *open literature*, ingestion of methamidophos has been shown to result in delayed peripheral neuropathy in humans. Similarly, adult hens developed poly neuropathy but only after ingestion of doses 12-16 times the $LD_{50}$. The HIARC recognized that the dose levels causing delayed neuropathy in humans are not well characterized. Exposures occurred at high doses through accidental occupational poisoning, suicide attempts or ingestion of contaminated vegetables.

Based on the above summarized toxicological studies, the Hazard Identification Assessment Review Committee determined that there are toxicological endpoints of concern for methamidophos (see HED Document Nos. 012477 and 012921). All of the toxicity endpoints and doses for risk assessment were selected based upon the most sensitive toxic effect and derived from studies which used similar routes of exposure to those expected for possible human exposures. The information is shown in Table 2.

**Table 2. Methamidophos Endpoints Used For Risk Assessment**

| Exposure Scenario | NOAEL for use in Risk Assessment (Study ) | Uncertainty Factor | Endpoint |
|---|---|---|---|
| **Acute Dietary** | 0.3 mg/kg/day (Acute Neurotoxicity-rat)<br><br>aRfD = 0.003 mg/kg/day<br>aPAD = 0.001 mg/kg/day | 300* | Plasma, erythrocyte and brain ChE inhibition |
| **Chronic Dietary Adjusted RfD = 0.0001 mg/kg/day** | 0.03 mg/kg/day (8 week toxicity-rat)<br><br>aRfD = 0.0003 mg/kg/day<br>aPAD = 0.0001 mg/kg/day | 300* | Brain ChE inhibition |
| **Short-Term (1-7 days)** | 0.75 mg/kg/day<br>(21 day dermal-rat) | 100 | Brain ChE inhibition |
| **Intermediate-Term Exposure (1 week to several months)** | 0.75 mg/kg/day<br>(21-day dermal-rat) | 100 | Brain ChE inhibition |
| **Long-Term Exposure (several months to lifetime)** | Not applicable<br><br>The use pattern does not indicate potential long-term dermal or inhalation exposure. | N/A | N/A |
| **Inhalation Exposure (any duration)** | 0.001 mg/L<br><br>(90-day inhalation- rat) | 100 | plasma, brain and erythrocyte ChE inhibition |
| **Carcinogenic** | Methamidophos has been classified as a "not likely" human carcinogen. Risk assessment not required. | N/A | N/A |
| **Aggregate Assessment** | The dermal and inhalation MOE's may be combined to obtain a total MOE since a common toxicological endpoint (cholinesterase inhibition) was observed. | N/A | N/A |
| FQPA Considerations | For methamidophos the 10-fold uncertainty factor to account for the protection of infants and children has been reduced to 3X. Thus, for all scenarios, MOEs equal to or greater than 300 are appropriate. | N/A | N/A |

NOAEL - No Observable Effect Level, ChE = Cholinesterase, MOE = Margin of Exposure, N/A = not applicable

Note that only short- and intermediate- term exposure/risk assessments are evaluated in this document. Exposures from the uses of methamidophos were determined to be of an intermittent nature (i.e., the frequency and duration of these exposures do not exhibit a chronic exposure pattern); therefore long-term assessment is not required.

*The 300x safety factor which includes a 3X factor for FQPA, is applicable for dietary exposures (residential exposure to methamidophos do not occur).

# 4 Exposure Assessment

## 4.1 Summary of Registered Uses

Methamidophos (O,S-dimethyl phosphoramidothioate) is a restricted use pesticide that is used as an acaricide/insecticide in agricultural settings. Methamidophos is formulated as a liquid product containing 40 percent active ingredient. The product is known as Monitor 4. As a result of an agreement between the registrant of methamidophos and EPA, methamidophos currently may be applied only to potatoes, tomatoes, and cotton. All uses other than potatoes and cotton have been deleted from the FIFRA Section 3 labels as of December 31, 1997. Under the same agreement, the use patterns for tomatoes are limited to FIFRA Section 24 (c) labels in 11 States. The registrant has submitted a petition for import tolerances on squash, strawberries and peppers which will be included in this risk assessment; the petition has not been reviewed. For the dietary risk assessment, anticipated residue were calculated using available FDA or USDA monitoring data. There is an existing tolerance for methamidophos on peppers, but none has been established for the other two commodities

Methamidophos can be applied aerially, by groundboom sprayer, and by sprinkler irrigation (i.e., chemigation) to potatoes only. For potatoes, the maximum application rate is 1.0 lb ai/acre (range = 0.5 to 1.0 lb ai/acre), and applications are made according to a 7 to 10 day preventative program or “as necessary”. Applications to potatoes must not be made later than 14 days before harvest. For cotton, the maximum application rate is 1.0 lb ai/acre (range = 0.1 to 1.0 lb ai/acre), and 1 to 2 applications can be made per season. The preharvest application interval for cotton is 50 days. For tomatoes, the maximum application rate is also 1.0 lb ai/acre (range 0.75 to 1.0 lb ai/acre) and applications can be made at 5 to 7 day intervals, as necessary, up to 7 days before harvest.

## 4.2 Dietary Exposure

Potential exposure to methamidophos residues in the diet occurs through food and water. Data supporting food exposure are adequate and are summarized in the Residue and Product Chemistry Chapters (Attachment 2). Exposure to methamidophos residues in ground and surface water was estimated using conservative modeling techniques; available monitoring data were assessed but were not considered adequate for quantitative risk assessment purposes

### 4.2.1 Food Exposure

The chemistry database is essentially complete. Based on the available plant metabolism data, the methamidophos residue of concern in plant commodities is the parent, methamidophos. Acceptable goat and hen metabolism studies have been submitted and evaluated. The livestock metabolism data indicate that no detectable residues of concern are likely to be present in eggs, milk, and livestock tissues. With regard to livestock, a 40 CFR 180.6(a)(3) [Category 3] situation exists i.e., no expectation of finite residues in meat, milk, poultry, or eggs. Therefore, no tolerances on animal commodities are required.

Adequate methods are available for the enforcement of established tolerances. The Pesticide Analytical Manual (PAM) Volume II lists Method I, a GLC method employing thermionic detection, as well as Method A, a confirmatory TLC method.

Codex MRLs have been established for residues of methamidophos *per se*.

Pending label amendments for some crops, adequate field trial data are available to reassess the established tolerances for cottonseed, potatoes, and tomatoes. The available data suggest that the tolerance levels for cottonseed and tomato should be raised to 0.2 ppm and 2.0 ppm, respectively. A tolerance for residues of methamidophos in/on cotton gin byproducts must be proposed. The available data support a tolerance level of 10 ppm (see Table 3.).

The registrants are not supporting use of methamidophos on Brussels sprouts, cauliflower, celery, and lettuce. Because there are registered acephate uses on these crops, methamidophos tolerances for these crops should be moved to 40 CFR §180.315(c). The tolerance expression in this section should read: "Tolerances are established for residues of methamidophos in or on the following raw agricultural commodities as a result of the application of acephate:". Additionally, the basic producer of acephate (Valent U.S.A. Corporation) has indicated that they will be supporting use of acephate on the following food/feed crops which were not originally on the methamidophos labels: beans (snap, dry, and lima); cranberries; and peppermint/spearmint. Therefore, tolerances for residues of methamidophos in/on these commodities resulting from use of acephate should also be established under 40 CFR §180.315(c). These crops have been considered in the methamidophos/acephate aggregate risk assessment.

The following tolerances should be revoked as the registrants are not supporting methamidophos uses and there are no registered acephate uses on these commodities: beets, sugar, roots; beets, sugar, tops; broccoli; cabbage; cucumbers; eggplant; and melons. These commodities were not included in the methamidophos risk assessment.

Additionally, Valent U.S.A. Corporation has submitted import tolerance petitions in support of uses of methamidophos on squash, strawberries, and peppers (PP#9E5040). There is an existing tolerance for methamidophos on peppers, but none has been established for the latter two commodities. The dietary risk assessment included these proposed uses.

HED conducts dietary risk assessments using the Dietary Exposure Evaluation Model (DEEM$^{TM}$), which incorporates consumption data generated in USDA's Continuing Survey of Food Intakes by Individuals (CSFII), 1989-1992. For chronic dietary risk assessments, the three day average of consumption for each sub-population is combined with residues in commodities to determine average exposure in mg/kg/day. For acute dietary risk assessments, the entire distribution of single day food consumption events is combined with either a single residue level (deterministic analysis) or a distribution of residues (probabilistic analysis, referred to as "Monte Carlo") to obtain a distribution of exposure in mg/kg/day. For deterministic (Tier 1) analyses, the Agency regulates at the 95$^{th}$ percentile of exposure; when probabilistic assessments are conducted, the Agency regulates at the 99.9th percentile of exposure.

Acute and chronic dietary exposure to methamidophos (including methamidophos residues from application of methamidophos only, not acephate) result in risk estimates that are below the Agency's level of concern (<100% of the aPAD and cPAD, respectively). Residue refinements including anticipated residues generated from field trial and monitoring data, adjustments for percent crop treated, washing and cooking factors and a probabilistic/Monte Carlo acute analyses were utilized. Monitoring data for methamidophos were generated through the USDA Pesticide Data program (PDP) for potatoes and tomatoes and through the FDA Surveillance Monitoring Program for peppers, squash, and strawberries. Field trial (FT) data were used for cotton (see Table 3). Applying all of these refinements, the most highly exposed population subgroup for both acute and chronic dietary risk was children 1-6 years with a percent chronic population adjusted dose (% cPAD) of 15 and a %aPAD of 72% at the 99.9th percentile exposure. Chronic exposure to the general U.S. population is 7 %cPAD and 55% of the aPAD at the 99.9th percentile. Dietary risks are summarized in Table 4.

**Table 3. Summary of Data Used for Methamidophos in Acute Monte Carlo Assessment**

| Commodity | Data Source PDP/FDA/FT |
|---|---|
| **Methamidophos application** | |
| **Cottonseed meal/oil** | FT |
| **Potatoes** | PDP (1994-1995) |
| **Tomatoes** | PDP (1996-1997) |
| **Squash** | FDA (1996-1998) |
| **Strawberries** | FDA (1996-1998) |
| **Peppers, Bell** | FDA (1993-1998) |
| **Peppers, Non-Bell** | FDA (1993-1998) |
| **Acephate application** | |
| **Succulent Beans** | PDP (1994-1997) |
| **Dry Beans** | FT |
| **Brussels sprouts** | FT |
| **Cauliflower** | FDA (1993-1998) |
| **Celery** | PDP (1994) |
| **Cottonseed meal/oil** | FT |
| **Cranberries** | FT |
| **Head Lettuce** | PDP (1994) |
| **Macadamia Nuts** | FT |
| **Mint** | FT |
| **Peanut (all food forms)** | FT |
| **Pepper Bell** | FDA(1993-1998) |
| **Pepper, Non Bell** | FDA(1993-1998) |
| **Soybean** | FT |

**Table 4. Acute and Chronic Dietary Risk (methamidophos application only)**

| Population Subgroup | Acute (99.9%-ile) | | Chronic | |
|---|---|---|---|---|
| | Exposure (mg/kg/day) | % aPAD | Exposure (mg/kg/day) | % cPAD |
| General U.S. Population | 0.000546 | 55 | 0.000007 | 7 |
| All Infants (<1 yr) | 0.000374 | 37 | 0.000004 | 4 |
| Children (1-6 yrs) | 0.000724 | 72 | 0.000015 | 15 |
| Children (7-12 yrs) | 0.000691 | 69 | 0.000011 | 11 |
| Females (13-50 yrs) | 0.000497 | 50 | 0.000006 | 6 |

[1] The acute population adjusted dose (aPAD) is 0.001 mg/kg/day and the chronic population adjusted dose (cPAD) is 0.0001 mg/kg/day. Refer to text pgs. 2-3 for details on endpoint selection.

### 4.2.2 Drinking Water

Limited drinking water monitoring data are available for methamidophos. Therefore, the surface and ground water assessments were based on modeling predictions. Very little surface water monitoring data have been collected and reported to the STORET system. Data were collected between 1977 and 1996; no detections of methamidophos were reported. NAWQA is not currently analyzing for methamidophos.

#### 4.2.2.1 Surface Water

Tier II estimated environmental concentrations (EECs) for methamidophos used on cotton in Mississippi and on potatoes in Idaho were determined using PRZM-EXAMS because these were scenarios for which the label information was most complete. The PRZM scenarios were chosen to represent sites that were expected to produce greater mass pesticide runoff than 90% of the sites where the modeled crops may be grown greater than 90 of the time. Tier II analyses were not performed for methamidophos use on tomatoes because in Florida (the state with the greatest use of methamidophos on tomatoes) most tomato production is conducted using black plastic as a mulch. It is not appropriate to use the PRZM-EXAMS model to estimate pesticide runoff for this type of horticultural practice. Based on the modeling, concentrations of methamidophos are not likely to exceed 48 ppb for peak(acute) exposure and 0.9 ppb for mean (chronic) exposure.

#### 4.2.2.2 Ground Water

Methamidophos is not persistent under aerobic conditions; therefore, very little methamidophos is expected to leach to groundwater. Using the SCI-GROW model to estimate concentrations of methamidophos in ground water, **the calculated EECs for both the acute and chronic effect of methamidophos** resulting from the use with the maximum yearly total application (nine applications at 1.0 lb methamidophos/A/application on tomatoes in Florida) **is 0.028 *u*g/L.** A small amount of monitoring data collected between 1984 and 1993 are available. Four detections of methamidophos were reported. The U.S. Geological Survey National Water Quality Assessment NAWQA) program is not currently analyzing for methamidophos.

### 4.3 Occupational Exposure

Methamidophos (O,S-dimethyl phosphoramidothioate) is a restricted use acaricide/insecticide registered for use in agricultural settings only. Two active labels are registered for methamidophos, both are emulsifiable concentrates with 40 percent active ingredient (ai) sold under the name Monitor® 4. An agreement between the registrants and EPA resulted in the uses of methamidophos being limited to potatoes and cotton and the FIFRA 24© uses on tomatoes only. In addition to the use deletions, the registrants committed to implement closed mixing and loading systems for potatoes and cotton by December 1997, and for tomatoes by December 1999. There are no residential uses or products available for sale to homeowners.

Applications of methamidophos are made using ground or aerial (foliar) equipment. Ground applications are made by groundboom or in irrigation water (also known as chemigation). Chemigation applications are only allowed on potatoes. Aerial applications are made by fixed or rotary (helicopter) wing aircraft.

The Agency believes that those involved in the application can be exposed. These people are generically referred to as handlers and represent those who prepare spray solutions for use (i.e., referred to as mixer/loaders), mark field for aerial application (flagger) and those who actually make the applications by driving the groundboom tractor, piloting the airplane or other piece of application equipment (referred to as applicators). A summary of use pattern used in the occupational exposure assessment are shown in Table 5.

**Table 5. Summary of Use Patterns Information Relevant to Occupational Exposure/Risk Assessment**

| Crop | Application Type | Application Rate, lb ai/acre | Maximum seasonal application (lb ai or application/season), PHI |
|---|---|---|---|
| **Cotton** | Ground or Aerial (foliar) | 1 lb ai/A | max. seasonal rate not specified<br>50 day PHI |
| **Potato** | Ground (including chemigation) or Aerial (foliar) | 1 lb ai/A | 4.0 lb ai/A,<br>14 day PHI |
| **Tomato SLNs** | Ground or Aerial (foliar) | 0.75 to 1 lb ai/A | 2 to 9 lb ai/A/yr, (every 7-10 days), 7 to 14 day PHI |
| | | | States: AL, AR, CA, DE, FL, GA, IN, LA, MD, MI, OH, NC, NJ, PR, SC, TN, TX, VA |

### 4.3.1 Handler

The Agency has determined that there are potential exposures to mixers, loaders, applicators, and flaggers when using methamidophos. Based on the labels and crop-specific use information, the following scenarios for exposure were associated with the use of methamidophos:

(1a) mixing and loading of liquid formulation for aerial application (all crops) and chemigation application (potatoes only);
(1b) mixing/loading of liquid formulation for groundboom applications;
(2) applying sprays with a fixed-wing aircraft;
(3) applying sprays with a helicopter;*
(4) applying sprays with groundboom equipment; and
(5) flagging aerial spray applications.

*No chemical-specific exposure data were submitted for any scenario. PHED contains insufficient data for rotary-winged aircraft applications therefore, aerial application in this assessment is considered for fixed-wing aircraft only[4].

The Agency classifies these scenarios as short-term exposures (one-week or less) and intermediate-term exposures (one week to several months). Typically the Agency conducts separate assessments for exposures less than one week, and greater than one week, for pesticides with the use patterns previously described. However, the toxicity studies for methamidophos indicate that toxic effects are similar for these

periods, so they will be considered together.

Generally, the Agency prefers to use chemical- and scenario-specific data to assess occupational exposures. In the absence of these data, the Agency uses monitoring data from similar exposure scenarios that have been collected and incorporated into a system known as the Pesticide Handlers Exposure Database (PHED). Chemical-specific occupational exposure studies were not submitted for methamidophos.

PHED, a library of actual exposure monitoring data that can be used to analyze specific types of exposures for those individuals involved in the application of pesticides (e.g., mixer/loaders, applicators), was used for all of the quantitative risk assessments that were completed for methamidophos. This system has been in use worldwide since 1992 and was developed by a task force that includes the EPA, Health Canada, the California Department of Pesticide Regulation, and the pesticide industry. The scientific basis for PHED has long been accepted by these groups. PHED forms the backbone of the vast majority of handler risk assessments completed by the Agency. The system now contains data from approximately 1700 exposures which were monitored when individuals were making actual pesticide applications in a variety of settings.

The basis of PHED is that individual handler exposures are related to how an application is made and not the specific pesticide being applied. The aspects of an application that are thought to affect exposures include: the kinds of equipment involved in application; the nature of the product being used (e.g., formulation and packaging); the application parameters such as application rate and total pounds of active ingredient applied; and the devices used by an individual to protect themselves during an application (e.g., additional clothing, chemical-resistant gloves, and closed tractor cabs).

The values that are calculated using PHED are called unit exposures and are generally presented as milligrams (or 1/1000th of a gram) exposure of active ingredient per pound active ingredient applied. For example, if one makes similar groundboom applications of 10 pounds of pesticide A or B, the unit exposures (1/10th of the exposure from applying 10 pounds of active ingredient A or B) would be proportional to the total amount applied and not whether pesticide A or B was in the spray tank. Separate unit exposures are typically calculated for the different equipment types that can be used in applications (e.g., open-cab groundboom and airblast applications would have different unit exposures). Separate unit exposures are also calculated for varying protective measures used during application with the same equipment. For example, there are specific unit exposures for groundboom

applications for individuals wearing normal work clothing, wearing normal work clothing under coveralls and with gloves, and for making applications using a closed cab tractor. In cases where data are not complete, the Agency uses available data and standard measures of protection to estimate exposure levels. For example, the Agency believes that the use of a coverall or a pair of chemical-resistant gloves provide a certain amount of protection when worn. These levels of protection and similar exposure data are used to calculate exposures where directly applicable data are not complete.

Along with the exposure values considered in the risk assessment (obtained from PHED), other information is needed to calculate the risk. Values needed are application rates, number of acres treated per day, body weight, and frequency of application. Amount of active ingredient handled per day is based on the number of acres treated and the application rate. These values are coupled with the unit exposures to calculate the daily exposure to the worker.

Initially the Agency calculates the risk using the least amount of protective measures, which is called the baseline assessment. For those involved in applications this usually represents an individual's normal work clothing, i.e. long sleeve shirts, long pants, no gloves, and no respirator. If there is a concern at this level, the Agency would require the use of devices to lower the risk. The first kinds of devices we would require are referred to as personal protective equipment (PPE). PPE can include an extra layer of clothing, chemical-resistant gloves, and respirators. If concerns persist, then the Agency would require additional protective measures often described as engineering controls. Common examples of engineering controls include enclosed tractor cabs, closed loading systems, and gel packs. This approach is commonly referred to as a tiered approach, and is well established in the area of risk assessment.

Product labels generally specify a certain level of PPE. However because the labels for older products are generally not based on a risk assessment, the Agency must begin its assessment assuming baseline measures and increase those measures until an acceptable level is obtained. Therefore any proposed label modifications will be based on this risk assessment instead of standard label recommendations.

Toxicity studies are required to determine the endpoints (toxic effects) which could result from worker exposures to pesticides. Studies are completed reflecting the major routes of exposure for workers: dermal and inhalation. These studies also determine exposure levels at which the toxic effects occur, as well as the highest level at which the toxic effects are unlikely to occur, called the No Observed Adverse Effect Level

(NOAEL). The NOAEL is compared to worker exposure to determine the risk, expressed as a Margin of Exposure (MOE = NOAEL/exposure). To calculate risks, the higher the MOE, the less the concern over the use. Typically, for workers, the Agency has concerns for MOEs that are less than 100. The 100 accounts for differences between the animals used for the toxicity tests and people (inter-species extrapolation) as well as the differences that can occur among people (intra-species variability). Worker risk may result from short-term exposures (1 to 7 days), or from intermediate-term exposures (1 week to several months). For methamidophos, the dermal and inhalation endpoints are the same (brain, plasma, RBC ChE inhibition); therefore, their margins of exposure (MOEs) are combined.

Results indicate that only two scenarios obtain a combined MOE > 100. The scenarios are (4) Applying spray with groundboom (MOE = 130), and (5) Flagging aerial application (MOE = 630). Both require engineering controls (enclosed cab) to obtain these acceptable MOE's. . The combined MOE results for each scenario at each mitigation level are presented in Table 6 below:

**Table 6. Summary of Combined Dermal and Inhalation MOEs for Methamidophos Occupational Handler Exposure**

| Exposure Scenario | Baseline Combined MOE | PPE Combined MOE | Engineering Control Combined MOE |
|---|---|---|---|
| **Mixer/Loader** | | | |
| **(1a) Mixing/Loading Aerial/Chemigation** | 0.052 | 8 | 17 |
| **(1b) Mixing/Loading Groundboom** | 0.23 | 35 | 74 |
| **Applicator Exposure** | | | |
| **(2) Applying Spray with Fixed Wing Aircraft** | NA | NA | 29 |
| **(3) Applying Spray with Helicopter** | NA | NA | NA |
| **(4) Applying spray with Groundboom** | 41 | 58 | 130 |
| **Flagger Exposure** | | | |
| **(5) Flagging Aerial Spray Applications** | 13 | 14 | 630 |

The following issues must be considered when interpreting the results of the occupational handler/postapplication risk assessment.

- ❏ No chemical-specific handler exposure data were submitted. As a result, all analyses were completed using surrogate exposure data from PHED V1.1. Several handler assessments were completed using "low quality" PHED data due to the lack of higher quality data (see Exposure Scenario Table 12 for further details). The PHED unit exposure values used in the assessment range between the geometric mean and the median of the available exposure data.

- ❏ Several generic protection factors were used to calculate handler exposures. PPE protection factors (PF) include those representing a double layer of clothing (50 percent PF)), chemical resistant gloves (90 percent PF) and respiratory protection (80 percent PF) for use of a dust/mist respirator. Engineering controls are generally assigned a PF of 98 percent. The value used for respiratory protection is based on the *NIOSH Respirator Decision Logic* and the value for gloves is in the range that OSHA and NIOSH typically use.

- ❏ Flagging aerial applications with engineering control was calculated with the baseline exposure units and a protection factor (PF) of 98%. HED believes the more common engineering control would be to install a global positioning system to replace the flagger, thus eliminating this exposure scenario.

- ❏ No DFR study was conducted on cotton, therefore data from the tomato studies in GA and CA were averaged and used as a default dissipation rate.

- ❏ Because of the insufficient number of data points for fixed-wing, open-cockpit aircraft in the PHED, these data are not used either as a subset, or in combination with data from fixed-wing, closed-cockpit aircraft. Exposure from open-cockpit planes is considered qualitatively to present a potentially greater exposure to applicators than closed-cockpit, but the quantitative extent remains unknown until empirical data are generated. If the estimated MOE for application of a given pesticide using closed-cockpit data from PHED or a pesticide-specific exposure study is an order of magnitude larger than the acceptable MOE, then the use of an open-cockpit fixed-wing aircraft for application also should be acceptable.

### 4.3.2 Post-Application Exposure

The Agency generally completes risk assessments for those individuals who can be exposed from entering previously treated areas to work (i.e., referred to as post-application exposures). The most common examples of these kinds of exposures are farmworker activities such as picking tomatoes.

Chemical-specific dislodgeable foliar residue studies did not contain worker exposure data. Default transfer coefficients were used to estimate potential exposures and doses for workers entering treated fields for various tasks. The default transfer coefficient values are based on published empirical data and are generally considered by HED to represent reasonable estimates of dermal exposure.

Three dislodgeable foliar residue (DFR) studies for methamidophos on tomatoes and potatoes were submitted to support reregistration. Because of the absence of additional DFR data for cotton treated with methamidophos, the tomato data were averaged and used as surrogate data for cotton. DFR studies are conducted to show the dissipation of a chemical on plant leaf/soil surfaces. The chemical is typically applied at the maximum rate and number of application allowed on the labels. The concentration of the chemical on the leaf surface (DFR) is used with transfer coefficients to calculate exposure to workers entering a treated field. The transfer coefficients represent an approximation of the total leaf surface area a worker would contact when performing a task (e.g., scouting, harvesting). Risks are then determined at various time intervals after application to determine appropriate reentry intervals (REI's), i.e., intervals when risks reach acceptable levels.

From these studies it appears that the restricted entry intervals (REIs) may have to be increased to protect workers. The current REIs listed on labels are WPS default values assigned in lieu of empirical data. For the current REIs of 48 to 72 hrs, the MOEs range between 4 and 20. The REIs calculated for this assessment range from 8 to 31 days (MOEs >100). Detailed information is shown in Tables 13 through 17 in this assessment

**Table 7. Summary of Calculated REIs for Methamidophos**

| Task | Crop | Application Rate (lb ai/A) | Interval after application at which MOE >100 (days) |
|---|---|---|---|
| **(1a)Scouting -early season** | Cotton | 1 | 18 |
| **(1b) Scouting -late season** | | | 31 |
| **(2) Harvest/dig tubers by hand** | Potatoes | 1 | 20 |
| **(3) Sort, pack Tubers** | | | 14 |
| **(4) Hand harvest, cut, transplant** | Tomatoes | 1 | 40 |
| **(5) Stake/tie, scout, irrigate** | | | 31 |

## 4.4 Residential Exposure

There are no products containing methamidophos that may be used in a residential setting. Therefore, no exposure and risk assessment is necessary for residential scenarios. The Agency recognizes there are many issues related to the use of agricultural chemicals and exposures in the general population; for example, the issues of spray drift and exposures to farmworker children. The Agency is in the process of developing guidance and procedures for characterizing these kinds of exposures. They are not addressed in this document. This guidance will be included in our upcoming revised SOPs for Residential Exposure Assessment.

Although there are no residential uses of methamidophos *per se*, the public may be exposed to methamidophos upon entering residential areas which have been previously treated with acephate. The available data indicated that residential acephate uses result in potential short-term dermal and oral acephate and methamidophos post-application residential exposures to the public. However, post-application inhalation exposures are not anticipated as a result of residential use of acephate.

It is anticipated that adults and children may primarily be exposed to acephate and methamidophos through their contact with acephate-treated turfgrass and soil. The analyses indicated that none of the acephate post-application residential exposure scenarios result in methamidophos exposures that exceed HED's level of concern (MOE range = 820 - 600,000). It should be noted that the residential SOPs specify that the residential exposure calculations are to be used on a screening basis.

The public may also be exposed to acephate and methamidophos upon entering recreational areas (golf courses) which have been previously treated with acephate. The possible post-application exposures are short-term dermal exposures; inhalation exposure is not expected. The recreational areas addressed in this assessment are golf courses.

The results indicated that MOEs for adult golfers' risks to methamidophos were 125,000 while the calculated MOEs for 13+ year-old golfers' risks to methamidophos were 78,100. (See Appendices A and B).

Detailed information, calculations and characterization of the occupational risk assessment can be found in Attachment 4.

### 4.5 Incident Data

An incident data report prepared for methamidophos (J. Blondell, 9/9/99, D258608) suggests that methamidophos poses one of the highest risks to workers of any organophosphate insecticide currently registered.

Based on Poison Control Center data methamidophos ranked second out of 28 cholinesterase-inhibiting insecticides on combined measures of hazard. Similarly for non-occupational cases (typically bystanders or other workers not directly involved in application), methamidophos ranked sixth. An earlier review of California data found that methamidophos had the highest risk of field worker poisoning per 1,000 applications but that this was influenced by large clusters. For example, in one incident 25 workers were poisoned in a cotton field that had been treated that morning, a clear violation of the required reentry waiting period. Overall combining California and Poison Control Center data rankings, led to methamidophos being ranked third (after mevinphos and carbofuran) for combined measures of hazard. The following databases were consulted for this preliminary report: OPP Incident Data System (IDS), Poison Control Centers, California Department of Pesticide Regulation, National Pesticide Telecommunications Network (NPTN).

Significant reductions in hazard to workers would result from cancellation of most uses. Where safer alternatives are not available, a full set of restrictive measures including posting, closed-mixing loading, reentry restrictions, and buffer zones to prevent drift to nearby workers or residential areas should be instituted.

# 5 FQPA Considerations

## 5.1 Aggregate Exposure

In examining aggregate exposure, FQPA directs EPA to take into account available information concerning exposures from pesticide residues in food and other exposures for which there is reliable information. These other exposures include drinking water and non-occupational exposures, e.g., to pesticides used in and around the home.

Methamidophos is a food use chemical. There are no residential uses of methamidophos; therefore, the considerations for aggregate exposure are those from food and water exposure. A dietary and water assessment which characterizes the aggregate exposure and risk for methamidophos residues from applications of methamidophos only (not acephate) was conducted. Also, since methamidophos is a metabolite of acephate, an aggregate risk assessment which determines the risk from methamidophos from applications of acephate and of methamidophos was also carried out.

### 5.1.1 Acute and Chronic DWLOCs//Aggregate Exposure/Risk (Methamidophos Residues from Methamidophos Applications only)

Drinking Water Levels of Comparison (DWLOCs) represent the maximum contribution to the human diet, in $\mu$g/L, that may be attributed to residues of a pesticide in drinking water after dietary exposure is subtracted from the aPAD or cPAD. In the case of methamidophos, there is no residential exposure. Acute and chronic DWLOCs for methamidophos were calculated based on dietary risk assessments using anticipated residues in food. These are presented in Tables 8 and 9. Comparisons are made between DWLOCs and the estimated concentrations of methamidophos in surface water and ground water generated via PRZM/EXAMS and SCI-GROW, respectively. If model estimate is less than the DWLOC, there is generally no drinking water concern.

**Table 8. Summary of Chronic DWLOC Calculations**

| Population Subgroup | cPAD (mg/kg/day) | Food Exposure (mg/kg/day) | Available Water Exposure (mg/kg/day) | DWLOC (ug/L) | PRZM/EXAMS (Overall mean) (ppb) | SCI-GROW (ug/L) |
|---|---|---|---|---|---|---|
| **U.S. Population** | 0.0001 | 0.000007 | 0.000093 | 3.3 | 0.9 | 0.028 |
| **Females 13-50 yrs** | 0.0001 | 0.000006 | 0.000094 | 2.8 | 0.9 | 0.028 |
| **Children 1-6 yr** | 0.0001 | 0.000015 | 0.000085 | 0.9 | 0.9 | 0.028 |
| **All Infants** | 0.0001 | 0.000004 | 0.000096 | 1.0 | 0.9 | 0.028 |

**Table 9. Summary of Acute DWLOC Calculations**

| Population Subgroup | aPAD (mg/kg/day) | Food Exposure (mg/kg/day) | Available Water Exposure (mg/kg/day) | DWLOC (ug/L) | PRZM/EXAMS (ppb) | SCI-GROW (ug/L) |
|---|---|---|---|---|---|---|
| **U.S. Population** | 0.001 | 0.000546 | 0.000454 | 16 | 48 | 0.028 |
| **Females 13-50 yrs** | 0.001 | 0.000497 | 0.000503 | 15 | 48 | 0.028 |
| **Children 1-6 yr** | 0.001 | 0.000724 | 0.000276 | 3 | 48 | 0.028 |
| **All Infants** | 0.001 | 0.000374 | 0.000626 | 6 | 48 | 0.028 |

**Chronic DWLOCs**. Upon comparison of the chronic DWLOCs with the environmental concentrations of methamidophos estimated using conservative modeling, surface water and ground water concentrations are equal to or less than the DWLOCs (Table 8) for all subpopulations. Therefore, there is no chronic dietary concern for methamidophos residues in drinking water.

**Acute DWLOCs**. Acute surface water concentrations estimated using conservative modeling exceed the acute DWLOCs; ground water estimates are less than the DWLOCs (Table 9). Thus, there appears to be a potential for methamidophos residues in surface water to occur at levels of concern. Uncertainties in the drinking water assessment include the lack of acceptable aerobic aquatic metabolism data. Aerobic aquatic metabolism data would increase the confidence in an exposure assessment by providing direct measurements of methamidophos behavior in aquatic environments.

### 5.1.2 Acute and Chronic Aggregate Exposure/Risk/DWLOCs (Combined Methamidophos Residues from Application of Both Methamidophos and Acephate)

For **chronic aggregate risk (food),** chronic exposures to methamidophos from application of acephate and application of methamidophos were combined and compared to the methamidophos reference dose. This assessment was conducted using anticipated residues and BEAD % crop treated information. Results of the chronic exposure analysis show that 23% of the cPAD is consumed for the U.S. population. The most significantly exposed subpopulation, children (1 to 6 years ) occupied 37.0% of the cPAD, respectively. The results indicate that HED has no concern for chronic aggregate exposure from food alone.

An **acute aggregate risk (food**) which considers methamidophos from application of acephate and methamidophos was also conducted. Residue refinements including anticipated residues generated from field trial and monitoring data, adjustments for percent crop treated, washing and cooking factors and a probabilistic/Monte Carlo acute analysis were utilized. Monitoring data for methamidophos (methamidophos application only) were generated through the USDA Pesticide Data program (PDP) for potatoes, and tomatoes and through the FDA Surveillance Monitoring Program for peppers, squash, and strawberries. Field trial (FT) data were used for cotton For methamidophos from the application of acephate, the acute estimates are based on USDA Pesticide Data Program (PDP) monitoring data for succulent beans, celery and lettuce; and FDA Surveillance Monitoring data for cauliflower and peppers (bell and non-bell). Monitoring data from the years 1994 through 1997 (PDP) and the years 1993 through 1998 (FDA) were considered. Monitoring data show that detectable residues of methamidophos are found (percent detects ranged from 1% (potatoes) - 34% (peppers)). Field trial data were used for Brussels sprouts, dry beans, cottonseed, cranberry, mint, macadamia nuts, peanuts, and soybean. Applying all of these refinements, the most highly exposed population subgroup was children 1-6 years with a %aPAD of 119%. For the general U.S. population, 79% of the aPAD was consumed. The results indicate that for infants and children, HED's level of concern is exceeded. Sensitivity analyses conducted show that tomatoes constitutes the majority of the dietary risk to methamidophos.

**Table 10. Aggregate Exposure: Summary of Methamidophos Acute and Chronic Non-Cancer Dietary Exposure and Risk Estimates**

| Population Subgroup | METHAMIDOPHOS | | | | | |
|---|---|---|---|---|---|---|
| | Acute (99.9%-ile) | | | | Chronic | |
| | All Commodities | | Excluding Tomatoes | | | |
| | Exposure (mg/kg/day) | % aPAD | Exposure (mg/kg/day) | % aPAD | Exposure (mg/kg/day) | %cPAD |
| General US Population | 0.000787 | 79 | 0.000308 | 31 | 0.000023 | 23 |
| All infants (<1 year) | 0.001074 | 107 | 0.000774 | 77 | 0.000031 | 31 |
| Children 1-6 years | 0.001194 | 119 | 0.000604 | 60 | 0.000037 | 37 |
| Children 7-12 years | 0.000976 | 98 | 0.000369 | 37 | 0.000030 | 30 |
| Females 13-50 years | 0.000653 | 65 | 0.000240 | 24 | 0.000021 | 21 |

1 Methamidophos - The acute Population Adjusted Dose (aPAD ) is 0.001 mg/kg/day ; the chronic PAD (cPAD) is 0.0001 mg/kg/day.

An **aggregate exposure assessment which quantifies risk from food and water** was conducted for chronic exposure only since HED has concerns for acute aggregate exposure from food alone, and because DWLOCs calculated for acute exposure from the application of methamidophos alone indicate that methamidophos residues in surface water may be of concern. Using the aggregate chronic food exposure (exposure which incorporates residues from application of methamidophos combined with residues from application of acephate), DWLOCs were calculated (Table 11). For children(1 to 6 years) and infants, the results indicated the potential for slight concern from surface water sources of drinking water.

**Table 11. Summary of Chronic DWLOC Calculations Incorporating Methamidophos Exposure from Applications of Methamidophos and Acephate**

| Population Subgroup | cPAD (mg/kg/day) | Food Exposure (mg/kg/day) | Available Water Exposure (mg/kg/day) | DWLOC (ug/L) | PRZM/EXAMS (Overall mean) (ppb) | SCI-GROW (ug/L) |
|---|---|---|---|---|---|---|
| **U.S. Population** | 0.0001 | 0.000023 | 0.000077 | 3 | 0.9 | 0.028 |
| **Females 13-50 yrs** | 0.0001 | 0.000021 | 0.000079 | 2 | 0.9 | 0.028 |
| **Children 1-6 yr** | 0.0001 | 0.000037 | 0.000063 | 0.6 | 0.9 | 0.028 |
| **All Infants** | 0.0001 | 0.000031 | 0.000069 | 0.7 | 0.9 | 0.028 |

## 5.2 Determination of Safety for Infants and Children

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for pre-and post-natal toxicity and the completeness of the database unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a MOE analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. EPA believes that reliable data support using the standard MOE and uncertainty factor (usually 100 for combined inter- and intra-species variability)) and not the additional tenfold MOE/uncertainty factor when EPA has a complete data base under existing guidelines and when the severity of the effect in infants or children or the potency or unusual toxic properties of a compound do not raise concerns regarding the adequacy of the standard MOE/safety factor.

**Susceptibility issues:** There was no indication of increased susceptibility of the offspring of rats or rabbits to pre- and or postnatal exposure to Methamidophos. In all studies examined, maternal or parental NOAELs were less than or equivalent to offspring NOAELs.

**Uncertainty factor:** The Committee determined that the **10x** factor to account for enhanced sensitivity of infants and children (as required by FQPA) **should be reduce to 3x** and is based on the following weight-of-the-evidence considerations:

1) Evidence of positive effects in the NTE assay in hens in Subchronic Toxicity Studies..

2) In studies from *open literature*, ingestion of methamidophos has been shown to result in delayed peripheral neuropathy in humans. Similarly, adult hens developed poly neuropathy but only after ingestion of doses 12-16 times the $LD_{50}$.

3) The HIARC recognized that the dose levels causing delayed neuropathy in humans are not well characterized. Exposures occurred at high doses through accidental occupational poisoning, suicide attempts or ingestion of contaminated vegetables.

4) Based on this evidence, a Developmental Neurotoxicity Study in Rats is **required**.

5) Developmental toxicity studies showed no increased susceptibility in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits.

6) A two generation reproduction toxicity study in rats showed no increased sensitivity in pup when compared to adults.

7) The toxicology data base is complete (i.e., no data gaps for standard Subdivision F Guidelines requirements).

8) The dietary food exposure assessment does not underestimate the potential exposure for infants and children from residues in food.

### 5.3 Cumulative Exposure To Substances with Common Mechanism of Toxicity

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

EPA does not have, at this time, available data to determine whether methamidophos has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this reregistration eligibility decision, therefore, EPA has not assumed that methamidophos has a common mechanism of toxicity with other substances.

However, the Agency has determined that methamidophos is a metabolite of a registered pesticide, acephate. Therefore, methamidophos residues resulting from applications of both acephate and methamidophos will be considered in a cumulative risk assessment and compared to appropriate toxicological endpoints for methamidophos. This is described to some extent in the aggregate exposure section of this risk assessment document.

## 5.4 Endocrine Disruption

The Food Quality Protection Act (FQPA; 1996) requires that EPA develop a screening program to determine whether certain substances (including all pesticides and inerts) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect....” EPA has been working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists to develop a screening and testing program as well as a priority setting scheme to implement this program. The Agency’s proposed Endocrine Disrupter Screening Program was published in the Federal Register of December 28, 1998 (63 FR71541). The Program uses a tiered approach and anticipates issuing a Priority List of chemicals and mixtures for Tier 1 screening in the year 2000. As the Agency proceeds with implementation of this program, further testing of [pesticide] and its end-use products for endocrine effects may be required.

**Table 12. Exposure Scenario Descriptions for the Use of Methamidophos**

| (Number) Exposure Scenario | Data Source | Standard Assumptions[a] (8-hr work day) | Comments[b] |
|---|---|---|---|
| **Mixer/Loader Descriptors** | | | |
| **(1a) Mixing/ Loading of Liquid Formulation for Aerial Application and Chemigation (i.e., sprinkler irrigation** | PHED V1.1 | 350 acres | **Baseline:** Hands, dermal, and inhalation - acceptable grades. Hands = 53 replicates; dermal = 75 to 122 replicates; inhalation = 85 replicates. High confidence in hands, dermal, and inhalation data. Single layer, no gloves for dermal. **PPE:** Hands, dermal, and inhalation - acceptable grades. Hands = 59 replicates; dermal = 72 to 122 replicates; inhalation = 85 replicates. High confidence in hands, dermal, and inhalation data. Maximum PPE values calculated from PHED data using a 50% protection factor for the addition of coveralls; a 80% protection factor was used for inhalation PPE. Double layer, gloves for dermal. **Engineering Controls (closed mixing)** Hands, dermal, and inhalation - acceptable grades. Hands = 31 replicates; dermal = 16 to 22 replicates; inhalation = 27 replicates. High confidence in hands, dermal, and inhalation data. Single layer, **gloves** for dermal. |
| **(1b) Mixing/ Loading of Liquid Formulation for Groundboom Applications** | PHED V1.1 | 80 acres | |
| **Applicator Descriptors** | | | |
| **(2) Applying Sprays with a Fixed-Wing Aircraft** | PHED V1.1 | 350 acres | **Baseline:** Not feasible, see Characterization Section 4.c.i **PPE:** Not Feasible **Engineering Controls (enclosed cockpit):** "Best Available" grades: Hands = acceptable grades; dermal and inhalation = ABC grades. Hands = 34 replicates; dermal = 24 to 48 replicates; inhalation = 23 replicates. Medium confidence in hands, dermal and inhalation data. Single layer, no gloves for dermal. |
| **(3) Applying Sprays with Helicopter** | PHED V1.1 | 350 acres. | **Baseline:** Not Feasible **PPE:** Not Feasible **Engineering Controls (closed cockpit):** *Aerial application in this assessment is assumed to be by fixed wing aircraft*. |

| (Number) Exposure Scenario | Data Source | Standard Assumptions[a] (8-hr work day) | Comments[b] |
|---|---|---|---|
| **(4) Applying Sprays with Groundboom Equipment** | PHED V1.1 | 80 acres | **Baseline:** Hands, dermal, and inhalation = acceptable grades. Hands = 29 replicates; dermal = 32 to 42 replicates; inhalation = 22 replicates. High confidence in hands, dermal and inhalation data. Single layer, no gloves for dermal.<br>**PPE:** Hands = ABC grades; dermal, and inhalation = acceptable grades. Hands = 21 replicates; dermal = 32 to 42 replicates; inhalation = 22 replicates. High confidence in hands, dermal and inhalation data. Maximum PPE values calculated from PHED data using a 50% protection factor for the addition of coveralls; a 80% protection factor was used for inhalation PPE. Double layer, no gloves for dermal.<br>**Engineering Controls (closed cab):** Hands = ABC grades; dermal = ABC grades; inhalation = acceptable grades. Hands = 16 replicates; dermal = 20 to 31 replicates; inhalation = 16 replicates. Medium confidence in hands and dermal; high confidence in inhalation. Single layer, no gloves for dermal. |
| **Flagger Descriptors** | | | |
| **(5) Flagging Aerial Spray Applications** | PHED V1.1 | 350 acres | **Baseline:** Hands, dermal, and inhalation = acceptable grades. Hands = 16 replicates; dermal = 16 to 18 replicates; inhalation =18 replicates. High confidence in hands, dermal and inhalation data. Single layer, no gloves for dermal.<br>**PPE:** Hands, dermal, and inhalation = acceptable grades. Hands = 16 replicates; dermal = 16 to 18 replicates; inhalation = 18 replicates. High confidence in hands, dermal, and inhalation data. Maximum PPE values calculated from PHED data using a 50% protection factor (PF) on non-hand dermal data to simulate the use of coveralls (double layer) and a 80% PF on inhalation data to simulate the use of a respirator. No gloves for dermal.<br>**Engineering Controls:** Same as Baseline values, using a 98%protection factor to account for enclosed vehicle engineering control. |

**Table 13. Estimates of Postapplication Exposure and Risk to Workers Dig/Harvest by Hand (TC = 10,000 $cm^2$/hr) Following Applications of Methamidophos to Potatoes (1.0 lb ai/acre)**

| DAT[a] | KS | | | MI | | | WA | | |
|---|---|---|---|---|---|---|---|---|---|
| | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Harvest Exposure[c] (mg/kg/day) | MOE[d] | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Harvest Exposure[c] (mg/kg/day) | MOE[d] | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Harvest Exposure[c] (mg/kg/day) | MOE[d] |
| **0** | 0.4839 | 0.5531 | 1 | 0.2668 | 0.3049 | 2 | 0.3075 | 0.352 | 2 |
| **1** | 0.3894 | 0.4450 | 2 | 0.1655 | 0.1891 | 4 | 0.2316 | 0.265 | 3 |
| **2** | 0.3133 | 0.3580 | 2 | 0.1026 | 0.1173 | 6 | 0.1744 | 0.199 | 4 |
| **3** | 0.2520 | 0.2880 | 3 | 0.06367 | 0.07276 | 10 | 0.1313 | 0.150 | 5 |
| **4** | 0.2028 | 0.2318 | 3 | 0.03949 | 0.04513 | 17 | 0.09891 | 0.113 | 7 |
| **5** | 0.1632 | 0.1865 | 4 | 0.02449 | 0.02799 | 27 | 0.07449 | 0.0851 | 9 |
| **6** | 0.1313 | 0.150 | 5 | 0.01519 | 0.01736 | 43 | 0.05610 | 0.0641 | 12 |
| **7** | 0.1056 | 0.1207 | 6 | 0.009422 | 0.01077 | 70 | 0.04224 | 0.0483 | 16 |
| **8** | 0.08497 | 0.09711 | 8 | **0.005844** | **0.00668** | **110** | 0.03181 | 0.0364 | 21 |
| **9** | 0.06837 | 0.07813 | 10 | - | - | - | 0.02396 | 0.0274 | 27 |
| **10** | 0.05501 | 0.06286 | 12 | - | - | - | 0.01804 | 0.0206 | 36 |
| **11** | 0.04426 | 0.05058 | 15 | - | - | - | 0.01359 | 0.0155 | 48 |
| **12** | 0.03561 | 0.04069 | 18 | - | - | - | 0.010232 | 0.0117 | 64 |
| **13** | 0.02865 | 0.03274 | 23 | - | - | - | 0.007706 | 0.00881 | 85 |
| **14** | 0.02305 | 0.02634 | 28 | - | - | - | **0.005803** | **0.00663** | **110** |
| **15** | 0.01855 | 0.02119 | 35 | - | - | - | - | - | - |
| **16** | 0.01492 | 0.01705 | 44 | - | - | - | - | - | - |
| **17** | 0.01200 | 0.01372 | 55 | - | - | - | - | - | - |
| **18** | 0.009658 | 0.01104 | 68 | - | - | - | - | - | - |
| **19** | 0.007771 | 0.008881 | 84 | - | - | - | - | - | - |
| **20** | **0.006252** | **0.007145** | **105** | - | - | - | - | - | - |

NOTE: Values rounded; calculations are based on spreadsheet analyses.

[a]Days After Treatment (DAT). Workers wearing long pants, long sleeved shirts and no gloves.

[b]Dislodgeable Foliar Residue (DFR) calculated by Versar using Excel® Spreadsheet and ANOVA.

[c]Harvest Exposure (mg/kg/day) = DFR ($\mu g/cm^2$) * Transfer Coefficient (10,000 $cm^2$/hr for potato harvest) * (8 hr/work day) * (1mg/1000 $\mu g$ conversion factor) ÷ 70 kg Body Weight.

[d]Dermal Short- and Intermediate-term MOE = $NOAEL_{dermal}$/ Exposure; where $NOAEL_{dermal}$ = 0.75 mg/kg/day. MOE of 100 is an acceptable margin of exposure.

**Table 14. Estimates of Postapplication Exposure and Risk to Workers Harvest by Hand (TC = 10,000 $cm^2$/hr) Following Applications of Methamidophos to Tomatoes (1.0 lb ai/acre).**

| DAT[a] | FL | | | GA | | | CA | | |
|---|---|---|---|---|---|---|---|---|---|
| | DFR (1lb ai/A) $\mu g/cm^2$ | Harvest Exposure (mg/kg/day) | MOE | DFR (1lb ai/A) $\mu g/cm^2$ | Harvest Exposure (mg/kg/day) | MOE | DFR (1lb ai/A) $\mu g/cm^2$ | Harvest Exposure (mg/kg/day) | MOE |
| **0** | 0.4657 | 0.532 | 1 | 0.5438 | 0.622 | 1 | 0.2646 | 0.302 | 2 |
| **1** | 0.4177 | 0.477 | 2 | 0.4269 | 0.488 | 2 | 0.2104 | 0.241 | 3 |
| **2** | 0.3746 | 0.428 | 2 | 0.3351 | 0.383 | 2 | 0.1673 | 0.191 | 4 |
| **3** | 0.3360 | 0.384 | 2 | 0.2631 | 0.301 | 2 | 0.1331 | 0.152 | 5 |
| **4** | 0.3013 | 0.344 | 2 | 0.2065 | 0.236 | 3 | 0.1058 | 0.121 | 6 |
| **5** | 0.2703 | 0.309 | 2 | 0.1621 | 0.185 | 4 | 0.08415 | 0.0962 | 8 |
| **6** | 0.2424 | 0.277 | 3 | 0.1273 | 0.145 | 5 | 0.06692 | 0.0765 | 10 |
| **7** | 0.2174 | 0.248 | 3 | 0.09990 | 0.114 | 7 | 0.05322 | 0.608 | 12 |
| **8** | 0.1950 | 0.223 | 3 | 0.07842 | 0.0896 | 8 | 0.04232 | 0.0484 | 16 |
| **9** | 0.1749 | 0.200 | 4 | 0.06156 | 0.0704 | 11 | 0.03366 | 0.0385 | 19 |
| **10** | 0.1569 | 0.179 | 4 | 0.04832 | 0.0552 | 14 | 0.02676 | 0.0306 | 25 |
| **11** | 0.1407 | 0.161 | 5 | 0.03793 | 0.0434 | 17 | 0.02128 | 0.0243 | 31 |
| **12** | 0.1262 | 0.144 | 5 | 0.02978 | 0.0340 | 22 | 0.01693 | 0.0193 | 39 |
| **13** | 0.1132 | 0.129 | 6 | 0.02338 | 0.0267 | 28 | 0.01346 | 0.0154 | 49 |
| **14** | 0.1015 | 0.116 | 6 | 0.01835 | 0.0210 | 36 | 0.01070 | 0.0122 | 61 |
| **15** | 0.09103 | 0.104 | 7 | 0.01440 | 0.0165 | 46 | 0.008512 | 0.00973 | 77 |
| **16** | 0.08165 | 0.0933 | 8 | 0.01131 | 0.0129 | 58 | 0.006769 | 0.00774 | 97 |
| **17** | 0.07323 | 0.0837 | 9 | 0.008877 | 0.0101 | 74 | **0.005383** | **0.00615** | **120** |
| **18** | 0.06568 | 0.0751 | 10 | 0.006968 | 0.00796 | 94 | - | - | - |
| **19** | 0.05891 | 0.0673 | 11 | **0.005470** | **0.00625** | **120** | - | - | - |
| **20** | 0.05283 | 0.0604 | 12 | - | - | - | - | - | - |
| **21** | 0.04738 | 0.0542 | 14 | - | - | - | - | - | - |
| **22** | 0.04250 | 0.0486 | 15 | - | - | - | - | - | - |
| **23** | 0.03812 | 0.0436 | 17 | - | - | - | - | - | - |
| **24** | 0.03419 | 0.0391 | 19 | - | - | - | - | - | - |
| **25** | 0.03066 | 0.0350 | 21 | - | - | - | - | - | - |
| **26** | 0.02750 | 0.0314 | 24 | - | - | - | - | - | - |
| **27** | 0.02466 | 0.0282 | 27 | - | - | - | - | - | - |
| **28** | 0.02212 | 0.0253 | 30 | - | - | - | - | - | - |
| **29** | 0.01984 | 0.0227 | 33 | - | - | - | - | - | - |
| **30** | 0.01780 | 0.0203 | 37 | - | - | - | - | - | - |
| **31** | 0.01596 | 0.0182 | 41 | - | - | - | - | - | - |

| DAT[a] | FL | | | GA | | | CA | | |
|---|---|---|---|---|---|---|---|---|---|
| | DFR (1lb ai/A) $\mu$g/cm$^2$ | Harvest Exposure (mg/kg/day) | MOE | DFR (1lb ai/A) $\mu$g/cm$^2$ | Harvest Exposure (mg/kg/day) | MOE | DFR (1lb ai/A) $\mu$g/cm$^2$ | Harvest Exposure (mg/kg/day) | MOE |
| **32** | 0.01431 | 0.0164 | 46 | - | - | - | - | - | - |
| **33** | 0.01284 | 0.0147 | 51 | - | - | - | - | - | - |
| **34** | 0.01151 | 0.0132 | 57 | - | - | - | - | - | - |
| **35** | 0.01033 | 0.0118 | 64 | - | - | - | - | - | - |
| **36** | 0.009263 | 0.0106 | 71 | - | - | - | - | - | - |
| **37** | 0.008308 | 0.00949 | 79 | - | - | - | - | - | - |
| **38** | 0.007451 | 0.00852 | 88 | - | - | - | - | - | - |
| **39** | 0.006683 | 0.00764 | 98 | - | - | - | - | - | - |
| **40** | 0.005994 | 0.00685 | **110** | - | - | - | - | - | - |

NOTE: Values rounded; calculations are based on spreadsheet analyses.

[a]Days After Treatment (DAT). Workers wearing long pants, long sleeved shirts and no gloves.

[b]Dislodgeable Foliar Residue (DFR) calculated by Versar using Excel® Spreadsheet and ANOVA.

[c]Harvest Exposure (mg/kg/day) = DFR ($\mu$g/cm$^2$) * Transfer Coefficient (10,000 cm$^2$/hr for tomato harvest) * (8 hr/work day) * (1mg/1000 $\mu$g conversion factor) ÷70 kg Body Weight.

[d]Dermal Short- and Intermediate-term MOE = $NOAEL_{dermal}$/ Exposure; where $NOAEL_{dermal}$ = 0.75 mg/kg/day. MOE of 100 is acceptable margin of exposure.

**Table 15. Estimates of Postapplication Exposure and Risk to Workers Sorting and Packing (Tc = 2,500 $cm^2$/hr) Following Applications of Methamidophos to Potatoes (1.0 lb ai/acre)**

| DAT[a] | KS | | | MI | | | WA | | |
|---|---|---|---|---|---|---|---|---|---|
| | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Harvest Exposure[c] (mg/kg/day) | MOE[d] | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Harvest Exposure[c] (mg/kg/day) | MOE[d] | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Harvest Exposure[c] (mg/kg/day) | MOE[d] |
| **0** | 0.4839 | 0.138 | 5 | 0.2668 | 0.0762 | 10 | 0.3075 | 0.0879 | 9 |
| **1** | 0.3894 | 0.111 | 7 | 0.1655 | 0.0473 | 16 | 0.2316 | 0.0662 | 11 |
| **2** | 0.3133 | 0.0895 | 8 | 0.1026 | 0.0293 | 26 | 0.1744 | 0.0498 | 15 |
| **3** | 0.2520 | 0.0720 | 10 | 0.06367 | 0.0182 | 41 | 0.1313 | 0.0375 | 20 |
| **4** | 0.2028 | 0.0579 | 13 | 0.03949 | 0.0113 | 66 | 0.09891 | 0.0283 | 27 |
| **5** | 0.1632 | 0.0466 | 16 | **0.02449** | **0.0070** | **107** | 0.07449 | 0.0213 | 35 |
| **6** | 0.1313 | 0.0375 | 20 | - | - | - | 0.05610 | 0.0160 | 47 |
| **7** | 0.1056 | 0.0302 | 25 | - | - | - | 0.04224 | 0.0121 | 62 |
| **8** | 0.08497 | 0.0243 | 31 | - | - | - | 0.03181 | 0.00909 | 83 |
| **9** | 0.06837 | 0.0195 | 38 | - | - | - | **0.02396** | **0.00685** | **110** |
| **10** | 0.05501 | 0.0157 | 48 | - | - | - | - | - | - |
| **11** | 0.04426 | 0.0126 | 59 | - | - | - | - | - | - |
| **12** | 0.03561 | 0.0102 | 74 | - | - | - | - | - | - |
| **13** | 0.02865 | 0.00819 | 92 | - | - | - | - | - | - |
| **14** | **0.02305** | **0.00659** | **114** | - | - | - | - | - | - |

NOTE: Values rounded; calculations are based on spreadsheet analyses.

[a]Days After Treatment (DAT). Workers wearing long pants, long sleeved shirts and no gloves.

[b]Dislodgeable Foliar Residue (DFR) calculated by Versar using Excel® Spreadsheet and ANOVA.

[c]Harvest Exposure (mg/kg/day) = DFR ($\mu g/cm^2$) * Transfer Coefficient (2,500 $cm^2$/hr for potato sorting/packing) * (8 hr/work day) * (1mg/1000 $\mu g$ conversion factor) ÷70 kg Body Weight.

[d]Dermal Short- and Intermediate-term MOE = $NOAEL_{dermal}$/ Exposure; where $NOAEL_{dermal}$ = 0.75 mg/kg/day. MOE of 100 is an acceptable margin of exposure.

**Table 16. Estimates of Postapplication Exposure and Risk to Workers Harvest by Stake/Tie/Scout/Irrigate (Tc = 4,000 $cm^2$/hr) Following Applications of Methamidophos to Tomatoes (1.0 lb ai/acre)**

| DAT[a] | FL | | | GA | | | CA | | |
|---|---|---|---|---|---|---|---|---|---|
| | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Stake/Tie Exposure[c] (mg/kg/day) | MOE[d] | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Stake/Tie Exposure[c] (mg/kg/day) | MOE[d] | DFR (1lb ai/A)[b] $\mu g/cm^2$ | Stake/Tie Exposure[c] (mg/kg/day) | MOE[d] |
| **0** | 0.4657 | 0.213 | 4 | 0.5438 | 0.249 | 3 | 0.2646 | 0.121 | 6 |
| **1** | 0.4177 | 0.191 | 4 | 0.4269 | 0.195 | 4 | 0.2104 | 0.0962 | 8 |
| **2** | 0.3746 | 0.171 | 4 | 0.3351 | 0.153 | 5 | 0.1673 | 0.0765 | 10 |
| **3** | 0.3360 | 0.154 | 5 | 0.2631 | 0.120 | 6 | 0.1331 | 0.0608 | 12 |
| **4** | 0.3013 | 0.138 | 5 | 0.2065 | 0.0944 | 8 | 0.1058 | 0.0484 | 16 |
| **5** | 0.2703 | 0.124 | 6 | 0.1621 | 0.0741 | 10 | 0.08415 | 0.0385 | 19 |
| **6** | 0.2424 | 0.111 | 7 | 0.1273 | 0.0582 | 13 | 0.06692 | 0.0306 | 25 |
| **7** | 0.2174 | 0.0994 | 8 | 0.09990 | 0.0457 | 16 | 0.05322 | 0.0243 | 31 |
| **8** | 0.1950 | 0.0891 | 8 | 0.07842 | 0.0358 | 21 | 0.04232 | 0.0193 | 39 |
| **9** | 0.1749 | 0.0799 | 9 | 0.06156 | 0.0281 | 27 | 0.03366 | 0.0154 | 49 |
| **10** | 0.1569 | 0.0717 | 10 | 0.04832 | 0.0221 | 34 | 0.02676 | 0.0122 | 61 |
| **11** | 0.1407 | 0.0643 | 12 | 0.03793 | 0.0173 | 43 | 0.02128 | 0.0097 | 77 |
| **12** | 0.1262 | 0.0577 | 13 | 0.02978 | 0.0136 | 55 | 0.01693 | 0.0077 | 97 |
| **13** | 0.1132 | 0.0517 | 14 | 0.02338 | 0.0107 | 70 | **0.01346** | **0.0062** | **122** |
| **14** | 0.1015 | 0.0464 | 16 | 0.01835 | 0.0084 | 89 | - | - | - |
| **15** | 0.09103 | 0.0416 | 18 | **0.01440** | **0.0066** | **114** | - | - | - |
| **16** | 0.08165 | 0.0373 | 20 | - | - | - | - | - | - |
| **17** | 0.07323 | 0.0335 | 22 | - | - | - | - | - | - |
| **18** | 0.06568 | 0.0300 | 25 | - | - | - | - | - | - |
| **19** | 0.05891 | 0.0269 | 28 | - | - | - | - | - | - |
| **20** | 0.05283 | 0.0242 | 31 | - | - | - | - | - | - |
| **21** | 0.04738 | 0.0217 | 35 | - | - | - | - | - | - |
| **22** | 0.04250 | 0.0194 | 39 | - | - | - | - | - | - |
| **23** | 0.03812 | 0.0174 | 43 | - | - | - | - | - | - |
| **24** | 0.03419 | 0.0156 | 48 | - | - | - | - | - | - |
| **25** | 0.03066 | 0.0140 | 54 | - | - | - | - | - | - |

| DAT[a] | FL | | | GA | | | CA | | |
|---|---|---|---|---|---|---|---|---|---|
| | DFR (1lb ai/A)[b] $\mu$g/cm$^2$ | Stake/Tie Exposure[c] (mg/kg/day) | MOE[d] | DFR (1lb ai/A)[b] $\mu$g/cm$^2$ | Stake/Tie Exposure[c] (mg/kg/day) | MOE[d] | DFR (1lb ai/A)[b] $\mu$g/cm$^2$ | Stake/Tie Exposure[c] (mg/kg/day) | MOE[d] |
| **26** | 0.02750 | 0.0126 | 60 | - | - | - | - | - | - |
| **27** | 0.02466 | 0.0113 | 67 | - | - | - | - | - | - |
| **28** | 0.02212 | 0.0101 | 74 | - | - | - | - | - | - |
| **29** | 0.01984 | 0.0091 | 83 | - | - | - | - | - | - |
| **30** | 0.01780 | 0.0081 | 92 | - | - | - | - | - | - |
| **31** | **0.01596** | **0.0073** | **103** | - | - | - | - | - | - |

NOTE: Values rounded; calculations are based on spreadsheet analyses.

[a]Days After Treatment (DAT). Workers wearing long pants, long sleeved shirts and no gloves.

[b]Dislodgeable Foliar Residue (DFR) calculated by Versar using Excel® Spreadsheet and ANOVA for application of 1 lb ai per acre.

[c]Stake/Tie Exposure (mg/kg/day) = DFR ($\mu$g/cm$^2$) * Transfer Coefficient (4,000 cm$^2$/hr for tomato Scout/tie/stake/irrigate tomatoes) * (8 hr/work day) * (1mg/1000 $\mu$g conversion factor) ÷70 kg Body Weight.

[d]Dermal Short- and Intermediate-term MOE = $NOAEL_{dermal}$/ Exposure; where $NOAEL_{dermal}$ = 0.75 mg/kg/day. MOE of 100 is acceptable margin of exposure.

**Table 17. REIs calculated for Cotton dissipation using average slope from GA and CA tomatoes and average y-intercept**

| DAT[A] | Cotton (Tc = 1000) | | | Cotton (Tc = 4000) | |
|---|---|---|---|---|---|
| | DFR (1lb ai/A) $\mu$g/cm$^2$ | Early Season Scouting Exposure (mg/kg/day) | MOE | Late Season Scouting Exposure (mg/kg/day) | MOE |
| **0** | 0.4042 | 0.0462 | 16 | 0.185 | 4 |
| **1** | 0.3192 | 0.0365 | 21 | 0.146 | 5 |
| **2** | 0.2521 | 0.0288 | 26 | 0.115 | 7 |
| **3** | 0.1991 | 0.0228 | 33 | 0.0910 | 8 |
| **4** | 0.1573 | 0.0180 | 42 | 0.0719 | 10 |
| **5** | 0.1242 | 0.0142 | 53 | 0.0568 | 13 |
| **6** | 0.09809 | 0.0112 | 67 | 0.0448 | 17 |
| **7** | 0.07747 | 0.00885 | 85 | 0.0354 | 21 |
| **8** | **0.06119** | **0.00699** | **110** | 0.0280 | 27 |
| **9** | 0.04832 | - | - | 0.0221 | 34 |
| **10** | 0.03816 | - | - | 0.0174 | 43 |
| **11** | 0.03014 | - | - | 0.0138 | 54 |
| **12** | 0.02381 | - | - | 0.0109 | 69 |
| **13** | 0.01880 | - | - | 0.0086 | 87 |
| **14** | **0.01485** | **-** | **-** | **0.0068** | **110** |

NOTE: Values rounded; calculations are based on spreadsheet analyses.

[a]Days After Treatment (DAT). Workers wearing long pants, long sleeved shirts and no gloves.

[b]Dislodgeable Foliar Residue (DFR) calculated by Versar using Excel® Spreadsheet and ANOVA. Dissipation from average of CA and GA slope and intercepts on Tomatoes.

[c]Scouting Exposure (mg/kg/day) = DFR ($\mu$g/cm$^2$) * Transfer Coefficient (1000 or 4000 cm$^2$/hr for cotton scouting) * (8 hr/work day) * (1mg/1000 $\mu$g conversion factor) ÷70 kg Body Weight.

[d]Dermal Short- and Intermediate-term MOE = $NOAEL_{dermal}$/ Exposure; where $NOAEL_{dermal}$ = 0.75 mg/kg/day. MOE of 100 is an acceptable margin of exposure.

## Appendix A Acephate Non-Occupational (Residential) Exposure and Risk Assessment Tables (Short-Term Exposures)

**Table 1. Numerical Inputs for Non-Occupational (Residential) Handler Exposure to Acephate**

| Exposure Scenario | Application Rate[a] (lb ai/A or lb ai/gallons where noted) | Treated Area[b] (A/day or gallons/day where noted) | Residential Unit Values | |
|---|---|---|---|---|
| | | | Dermal[c] (mg / lb ai handled) | Inhalation[d] ($\mu$g / lb ai handled) |
| **Residential Exposure** | | | | |
| **(1) Mixing/Loading/Applying Wettable Powder Using a Low Pressure Hand Wand** | Ornamentals, Flowers, Shrubs, Trees, Fire Ants = 0.023 lb / gal | 2 gallons | 250 | 1100 |
| | Turf = 0.035 lb / gal | 2 gallons | 250 | 1100 |
| | Roses, Flowers, Shrubs, Trees = 0.0076 lb / gal (LUIS) | 2 gallons | 250 | 1100 |
| **(2) Mixing/Loading/Applying Using a Backpack Sprayer** | Ornamentals, Flowers, Shrubs, Trees, Fire Ants = 0.023 lb (4.5 grams) / gal | 2 gallons | 5.1 | 30 |
| | Turf = 0.035 lb / gal | 2 gallons | 5.1 | 30 |
| | Roses, Flowers, Shrubs, Trees = 0.0076 lb / gal (LUIS) | 2 gallons | 5.1 | 30 |
| **(3a) Mixing/Loading/Applying Using a Hose-End Sprayer** | Ornamentals, Flowers, Shrubs, Trees = 0.023 lb / gal | 50 gallons | 30 | 9.5 |
| | Turf = 0.035 lb / gal | 50 gallons | 30 | 9.5 |
| | Roses, Flowers, Shrubs, Trees = 0.0076 lb / gal (LUIS) | 50 gallons | 30 | 9.5 |
| | Shade Trees = 0.013 lb / gal (LUIS) | 50 gallons | 30 | 9.5 |
| | Ornamentals and Turf = 0.058 lb / 1000 sq ft (LUIS) | 20,000 sq ft (0.5 A) | 30 | 9.5 |

| Exposure Scenario | Application Rate[a] (lb ai/A or lb ai/gallons where noted) | Treated Area[b] (A/day or gallons/day where noted) | Residential Unit Values | |
|---|---|---|---|---|
| | | | Dermal[c] (mg / lb ai handled) | Inhalation[d] ($\mu$g / lb ai handled) |
| **(3b) Mixing/Loading/Applying Using a Hose-End Sprayer [MRID # 405048-27]** | Shrubbery = 0.01175 lb / gal | 50 gallons | 480 | 150 |
| **(4) Mixing/Loading/Applying Using a Sprinkling Can** | Ornamentals, Flowers, Shrubs, Trees, Fire Ants = 0.023 lb / gal | 5 gallons | 30 | 9.5 |
| | Turf = 0.035 lb / gal | 5 gallons | 30 | 9.5 |
| | Roses, Flowers, Shrubs, Trees = 0.0076 lb / gal (LUIS) | 5 gallons | 30 | 9.5 |
| **(5) Loading/Applying Soluble Powder (dry) Concentrate by Hand/Handtool/Shaker Can** | Fire Ants = 0.0069 lb / mound | 7 mounds | 430 | 470 |
| **(6) Loading/Applying Granules by Shaker Can**<br><br>**(NOTE: Label #239-2472 specifies 3 shaker cups of 1.5% / 25 sq ft; 0.5 lb/1000 sq ft used as per registrant)** | Ornamentals = 0.5 lb / 1000 sq ft | 100 sq ft | 430 | 470 |
| | Roses = 0.1125 lb / 1000 sq ft | 5 sq ft / rose; 20 roses | 430 | 470 |
| **(7) Applying by Aerosol Can** | Crack & Crevice = 0.01 lb / can | 2 cans (32 oz) | 220 | 2400 |
| | Ornamentals = 0.03 lb / can | 2 cans (32 oz) | 220 | 2400 |

[a]Application rates are values found on currently registered labels, through Agency sources (LUIS) and from information provided by the registrant.

[b]Amounts of acreage treated per day are from the HED estimates of acreage that could be treated in a single day for each exposure scenario of concern, through other Agency sources (LUIS) and from information provided by the registrant.

[c]Baseline dermal unit exposure represents an individual's estimated exposure while wearing short pants, short sleeved shirt, no gloves, open mixing/loading.

[d]Baseline inhalation unit exposure represents no use of a respirator.

**Table 2: Exposure and Risks for Non-Occupational (Residential) Handlers of Acephate**

| RESIDENTIAL Exposure Scenario | Application Rate (lb ai/A or lb ai/gallons where noted) | Treated Area (A/day or gallons where noted) | Daily Exposure (mg/day)[a] | | Absorbed Daily Dose (mg/kg/day )[b] | | Separate MOEs[c] | | Combined MOEs[d] |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal | Inhalation | Dermal | Inhalation | Dermal | Inhalation | |
| **Residential Exposure** | | | | | | | | | |
| **(1) Mixing/Loading/Applying Wettable Powder Using a Low Pressure Hand Wand** | Ornamentals, Flowers, Shrubs, Trees, Fire Ants = 0.023 lb / gal | 2 gallons | 12 | 0.051 | 0.17 | 0.00073 | 70 | 190 | 53 |
| | Turf = 0.035 lb / gal | 2 gallons | 18 | 0.077 | 0.26 | 0.0011 | 46 | 130 | 33 |
| | Roses, Flowers, Shrubs, Trees = 0.0076 lb / gal (LUIS) | 2 gallons | 3.8 | 0.017 | 0.054 | 0.00024 | 220 | 580 | 160 |
| **(2) Mixing/Loading/Applying Using a Backpack Sprayer** | Ornamentals, Flowers, Shrubs, Trees, Fire Ants = 0.023 lb (4.5 grams) / gal | 2 gallons | 0.23 | 0.0014 | 0.0033 | 0.00002 | 3600 | 7000 | 2400 |
| | Turf = 0.035 lb / gal | 2 gallons | 0.36 | 0.0021 | 0.0051 | 0.00003 | 2400 | 4700 | 1600 |
| | Roses, Flowers, Shrubs, Trees = 0.0076 lb / gal (LUIS) | 2 gallons | 0.078 | 0.00046 | 0.0011 | 0.0000065 | 11000 | 22000 | 7100 |
| **(3a) Mixing/Loading/Applying Using a Hose-End Sprayer** | Ornamentals, Flowers, Shrubs, Trees = 0.023 lb / gal | 50 gallons | 35 | 0.011 | 0.50 | 0.00016 | 24 | 880 | 23 |
| | Turf = 0.035 lb / gal | 50 gallons | 53 | 0.017 | 0.76 | 0.00024 | 16 | 580 | 16 |

| RESIDENTIAL Exposure Scenario | Application Rate (lb ai/A or lb ai/gallons where noted) | Treated Area (A/day or gallons where noted) | Daily Exposure (mg/day)[a] | | Absorbed Daily Dose (mg/kg/day )[b] | | Separate MOEs[c] | | Combined MOEs[d] |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal | Inhalation | Dermal | Inhalation | Dermal | Inhalation | |
| | Roses, Flowers, Shrubs, Trees = 0.0076 lb / gal (LUIS) | 50 gallons | 11 | 0.0036 | 0.16 | 0.000051 | 75 | 2700 | 73 |
| | Shade Trees = 0.013 lb / gal (LUIS) | 50 gallons | 20 | 0.0062 | 0.29 | 0.000088 | 41 | 1600 | 40 |
| | Ornamentals and Turf = 0.058 lb / 1000 sq ft (LUIS) | 20,000 sq ft (0.5 A) | 35 | 0.011 | 0.50 | 0.00016 | 24 | 880 | 23 |
| **(3b) Mixing/Loading/Applying Using a Hose-End Sprayer [MRID # 405048-27]** | Shrubbery = 0.01175 lb / gal | 50 gallons | 280 | 0.088 | 4.0 | 0.0012 | 3.0 | 120 | 2.9 |
| **(4) Mixing/Loading/Applying Using Sprinkling Can** | Ornamentals, Flowers, Shrubs, Trees, Fire Ants = 0.023 lb / gal | 5 gallons | 3.5 | 0.0011 | 0.05 | 0.000016 | 240 | 8800 | 230 |
| | Turf = 0.035 lb / gal | 5 gallons | 5.3 | 0.0017 | 0.076 | 0.000024 | 160 | 5800 | 160 |
| | Roses, Flowers, Shrubs, Trees = 0.0076 lb / gal (LUIS) | 5 gallons | 1.1 | 0.00036 | 0.016 | 0.0000051 | 750 | 27000 | 730 |
| **(5) Loading/Applying Soluble Powder (dry) Concentrate by Hand/Handtool/Shaker Can** | Fire Ants = 0.0069 lb / mound | 7 mounds | 21 | 0.022 | 0.30 | 0.00031 | 40 | 450 | 37 |

| RESIDENTIAL Exposure Scenario | Application Rate (lb ai/A or lb ai/gallons where noted) | Treated Area (A/day or gallons where noted) | Daily Exposure (mg/day)[a] | | Absorbed Daily Dose (mg/kg/day )[b] | | Separate MOEs[c] | | Combined MOEs[d] |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal | Inhalation | Dermal | Inhalation | Dermal | Inhalation | |
| **(6) Loading/Applying Granules by Shaker Can**<br><br>**(NOTE: Label #239-2472 specifies 3 shaker cups of 1.5% / 25 sq ft; 0.5 lb/1000 sq ft used as per registrant)** | Ornamentals = 0.5 lb / 1000 sq ft | 100 sq ft | 22 | 0.024 | 0.31 | 0.00034 | 39 | 410 | 36 |
| | Roses = 0.5 lb / 1000 sq ft | 5 sq ft / rose; 20 roses | 22 | 0.024 | 0.31 | 0.00034 | 39 | 410 | 36 |
| **(7) Applying by Aerosol Can** | Crack & Crevice = 0.01 lb / can | 2 cans (32 oz) | 4.4 | 0.048 | 0.063 | 0.00069 | 190 | 200 | 97 |
| | Ornamentals = 0.03 lb / can | 2 cans (32 oz) | 13 | 0.14 | 0.19 | 0.002 | 63 | 70 | 33 |

[a]Daily Exposure (mg/day) = Application Rate (lb ai/A or lb ai/gallon) * Treated Area (A/day or gallons/day) * Unit Exposure Value (mg or $\mu$g exposure/ lb ai handled) *[ 1mg/1000$\mu$g (conversion factor if necessary)].

[b]Absorbed Daily Dose (mg/kg/day) = Daily Exposure (mg/day) * Absorption (1) ÷ Body Weight (70kg).

[c]MOE (unitless) = NOAEL (mg/kg/day) ÷ Absorbed Daily Dose (mg/kg/day). Where $NOAEL_{dermal}$= 12 mg/kg/day and $NOAEL_{inhalation}$= 0.14 mg/kg/day.

[d]Combined MOEs = $\frac{1}{\left(\frac{1}{\mathrm{MOE}derm} + \frac{1}{\mathrm{MOE}inhal}\right)}$; MOE of 100 is an acceptable margin of exposure.

**Table 3. Non-Occupational (Residential) Exposure Scenario Descriptions for the Use of Acephate**

| Exposure Scenario (Number) | Data Source | Standard Assumptions[a] | Comments[b, c] |
|---|---|---|---|
| (1) Mixing/Loading /Applying Wettable Powder Using a Low Pressure Hand Wand | PHED V1.1 | 2 gallons (per registrant; label modification required to reflect such) | **Residential:** Hand data are grade A, dermal data are C grade, and inhalation data are C grade. Hand = 15 replicates; dermal = 16 replicates; and inhalation = 16 replicates. High confidence in hand data . Medium confidence in inhalation and dermal data. A 90% protection factor was needed to "back calculate" a no glove unit exposure value from all non-detects. |
| (2) Mixing /Loading/Applying Using a Backpack Sprayer | PHED V1.1 | 2 gallons (per registrant; label modification required to reflect such) | **Residential:** Hand is grade C, dermal data are AB grades, and inhalation data are A grade. Hand = 11 replicates; dermal = 9-11 replicates and inhalation = 11 replicates. Low confidence in hand/dermal/ inhalation data. A 90% protection factor was needed to "back calculate" a no glove unit exposure value from all non-detects. |
| (3a) Mixing/Loading/Applying Using a Hose-End Sprayer | PHED V1.1 | 50 gallons of spray solution and 20,000 sq ft (0.5 acre) for turf | **Residential:** Dermal =C grade; Hands =E grade and inhalation =C grade. Hand = 8 replicates; Dermal = 8 replicates; and inhalation = 8 replicates. Low confidence in dermal, hand and inhalation data. |
| (3b) Mixing/Loading/Applying Using a Hose-End Sprayer | MRID # 405048-27 | 50 gallons | 5 replicates |
| (4) Mixing/ Loading /Applying Using Sprinkling Can | PHED V1.1 | 5 gallons | **Residential:** Dermal,=C grade; Hands =E grade and inhalation=C grade. Hand =8 replicates; Dermal = 8 replicates; and inhalation = 8 replicates. Low confidence in dermal, hand and inhalation data. |
| (5) Loading/Applying Soluble Powder (dry) Concentrate by Hand/Handtool/Shaker Can | PHED V1.1 | 7 mounds | No PHED data were available for this scenario; therefore, used the PHED data for the granular bait dispersed by hand scenario.<br><br>**Residential:** Dermal = ABC grades, Hand = ABC grades; dermal/hands = 16 replicates, Inhalation = ABC grades, inhalation = 16 replicates. Medium confidence in dermal and inhalation data. |

| Exposure Scenario (Number) | Data Source | Standard Assumptions[a] | Comments[b, c] |
|---|---|---|---|
| (6) Loading/Applying Granules by Shaker Can | PHED V1.1 | 100 sq ft and 5 sq ft/rose for 20 roses<br><br>NOTE: Label #239-2472 specifies 3 shaker cups of 1.5% / 25 sq ft; 0.5 lb/1000 sq ft used as per registrant; label modification required to reflect such | No PHED data were available for this scenario; therefore, used the PHED data for the granular bait dispersed by hand scenario.<br><br>**Residential:** Dermal = ABC grades, Hand = ABC grades; dermal/hands = 16 replicates, Inhalation = ABC grades, inhalation = 16 replicates. Medium confidence in dermal and inhalation data. |
| (7) Applying By Aerosol Can | PHED V1.1 | 2 cans (32 oz.) | **Residential:** Hands=A grade, dermal/inhalation=ABC . Hand = 15 replicates; dermal/inhalation = 30 replicates. Medium confidence in dermal and inhalation data, high confidence in hand data. |

[a]Some of the assumptions are from Standard Operating Procedures (SOPs) for Residential Exposure Assessment.

[b]These grades are based on Quality Assurance/Quality Control data provided as part of the exposure studies. A replicate refers to data acquired during one complete work cycle. All handler exposure assessments in this document are based on the "Best Available" data as defined by HED SOP for meeting Subdivision U Guidelines (i.e., completing exposure assessments.) Best available grades are assigned as follows: matrices with grades A and B data (which is defined as acceptable grade data) and a minimum of 15 replicates; if not available, then grades A, B, and C data and a minimum of 15 replicates; if not available, then all data (all grades) regardless of the quality and number of replicates. High quality data with a protection factor take precedence over low quality data with no protection. Data confidence as reported in the Table refers to both the quality and the quantity (number of replicates) of data for each PHED run. Each study in PHED has been graded from A to E. A high confidence run is grades A and B data and 15 or more replicates per body part. Any combination of A and B grade data are listed as acceptable grades data in the tables. A medium confidence run is grades A, B, and C data and 15 or more replicates per body part. Any combination of A, B, and C grade data are listed as ABC grade data in the tables. A low confidence run is all grades (any run that includes D or E grade data) or has less than 15 replicates per body part.

[c]Clothing for residential scenarios is short pants, short-sleeved shirt, no gloves, open mixing/loading. Accounting for the use of PPE is not considered appropriate in residential risk assessments, as the Agency can only make recommendations to residential handlers regarding the use of PPE.

**Table 4. Post-Application Risks to Public Following Acephate Application to Turf in FL (5.0 lb ai/A – 2 applications) [ACEPHATE]**

| Scenario | Exposed Individual | Application Rate Per Treatment (AR) (lb ai/A)[a] | DFR (ug/cm$^2$)[b] | Grt (ug/cm$^2$)[c] | SRt (ug/g)[d] | Transfer Coefficient (Tc) (cm$^2$/hr) | Exposure Time (ET) (hrs/day) | Dermal Abs. (%) | Surface Area (SA) (cm$^2$/ event) | Freq. (FQ) (events / hr) | IgR (cm$^2$/day) or (mg/day)[e] | BW (kg) | ADD (mg/kg/day)[f] | MOE[g] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dermal exposure | Adult | 3.5 | 0.20 | - | - | 43,000 | 2 | 100 | - | - | - | 70 | 0.24 | 50 |
| | Child | | | | | 8,700 | | | | | | 15 | 0.23 | 52 |
| Hand-to-Mouth | Child | 3.5 | 0.20 | - | - | - | 2 | - | 350 | 1.56 | - | 15 | 0.014 | 36 |
| Turfgrass ingestion | Child | 3.5 | - | 7.8 | - | - | - | - | - | - | 25 | 15 | 0.013 | 38 |
| Incidental soil ingestion | Child | 3.5 | - | - | 21 | - | - | - | - | - | 100 | 15 | 0.00014 | 3600 |

[a]Maximum application rate for residential turf = 3.5 lb ai/acre.

[b]Dislodgeable foliar residue = 0.289 ug/cm$^2$ * 3.5 / 5.0 (ratio of application rates) = 0.20 ug/cm$^2$; Turf Transferable Residue (TTR) averaged from actual field measurements made following the second application of registrant's study and corrected for application rate of 3.5 lb ai/A.

[c]Grass residue (ug/cm$^2$) = [AR (lb ai/A) * fraction ai retained on foliage (20%) * 4.54E+8 ug/lb * 2.47E-8 A/cm$^2$] = 7.8 ug/cm$^2$.

[d]Soil residue (ug/g soil) = [AR (lb ai/A) * fraction ai not retained on foliage (80%) * 4.54E+8 ug/lb * 2.47E-8 A/cm$^2$ * 0.67 cm$^3$/g soil] = 21 ug/g soil.

[e]Ingestion rate: cm$^2$/day for grass ingestion, and mg/day for incidental soil ingestion.

[f]Average daily dose (ADD) (mg/kg/day)

Dermal exposure: = [DFR (ug/cm$^2$) * Tc (cm$^2$/hr) * mg/1,000 ug * ET ( hrs/day) * absorption factor (1.0)] / [BW (kg)];
Hand-to-mouth: = [DFR (ug/cm$^2$) * SA (cm$^2$/event) * FQ (events/hr) * mg/1,000 ug * ET (2 hrs/day)] / [BW (kg)];
Turfgrass ingestion: = [GRt (ug/cm$^2$) * IgR (cm$^2$/day) * mg/1,000 ug] / [BW (kg)]; and
Incidental soil ingestion: = [SRt (ug/g) * IgR (mg/day) * g/1,000,000 ug] / [BW (kg)].

[g]OE = NOAEL / ADD where acephate $NOAEL_{dermal}$= 12 mg/kg/day and acephate $NOAEL_{oraa}$ = 0.5 mg/kg/day ; the dermal NOAEL is used to calculate the dermal MOE and the acute oral NOAEL is used to calculate the hand-to-mouth, turfgrass ingestion and incidental soil ingestion MOEs. MOE of 100 is an acceptable margin of exposure.

**Table 5. Post-Application Risks to Public Following Acephate Application to Turf in FL (5.0 lb ai/A – 2 applications) [METHAMIDOPHOS]**

| Scenario | Exposed Individual | Application Rate Per Treatment (AR) (lb ai/A)[a] | DFR (ug/cm$^2$)[b] | GRt (ug/cm$^2$)[c] | SRt (ug/g)[d] | Transfer Coefficient (Tc) (cm$^2$/hr) | Exposure Time (ET) (hrs/day) | Dermal Abs. (%) | Surface Area (SA) (cm$^2$/ event) | Freq. (FQ) (events/ hr) | IgR (cm$^2$/day) or (mg/day)[e] | BW (kg) | ADD (mg/kg/day)[f] | MOE[g] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Dermal exposure** | Adult | 0.013 (3.5 lb ai/A acephate) | 0.00074 | - | - | 43,000 | 2 | 100 | - | - | - | 70 | 0.00091 | 820 |
| | Child | | | | | 8,700 | | | | | | 15 | 0.00086 | 870 |
| **Hand-to-Mouth** | Child | 0.013 (3.5 lb ai/A acephate) | 0.00074 | - | - | - | 2 | - | 350 | 1.56 | - | 15 | 0.000054 | 5600 |
| **Turfgrass ingestion** | Child | 0.013 (3.5 lb ai/A acephate) | - | 0.029 | - | - | - | - | - | - | 25 | 15 | 0.000048 | 6200 |
| **Incidental soil ingestion** | Child | 0.013 (3.5 lb ai/A acephate) | - | - | 0.078 | - | - | - | - | - | 100 | 15 | 0.0000005 | 600000 |

[a]Maximum application rate for residential turf = 3.5 lb ai/acre acephate * 0.00106 / 0.289 (ratio of methamidophos to acephate TTRs) = 0.013 lb ai/acre methamidophos.

[b]Dislodgeable foliar residue = 0.00106 ug/cm$^2$ * 3.5 / 5.0 (ratio of application rates) = 0.00074 ug/cm$^2$; Turf Transferable Residue (TTR) averaged from actual field measurements made following the second application of registrant's study and corrected for application rate of 3.5 lb ai/A.

[c]Grass residue (ug/cm$^2$) = [AR (lb ai/A) * fraction ai retained on foliage (20%) * 4.54E+8 ug/lb * 2.47E-8 A/cm$^2$] = 0.029 ug/cm$^2$.

[d]Soil residue (ug/g soil) = [AR (lb ai/A) * fraction ai not retained on foliage (80%) * 4.54E+8 ug/lb * 2.47E-8 A/cm$^2$ * 0.67 cm$^3$/g soil] = 0.078 ug/g soil.

[e]Ingestion rate: cm$^2$/day for grass ingestion, and mg/day for incidental soil ingestion.

[f]Average daily dose (ADD) (mg/kg/day)

Dermal exposure: = [DFR (ug/cm$^2$) * Tc (cm$^2$/hr) * mg/1,000 ug * ET ( hrs/day) * absorption factor (1.0)] / [BW (kg)];

Hand-to-mouth: = [DFR (ug/cm$^2$) * SA (cm$^2$/event) * FQ (events/hr) * mg/1,000 ug * ET (2 hrs/day)] / [BW (kg)];

Turfgrass ingestion: = [GRt (ug/cm$^2$) * IgR (cm$^2$/day) * mg/1,000 ug] / [BW (kg)]; and

Incidental soil ingestion: = [SRt (ug/g) * IgR (mg/day) * g/1,000,000 ug] / [BW (kg)].

[g]MOE = NOAEL / ADD where methamidophos $NOAEL_{dermal}$= 0.75 mg/kg/day and $NOAEL_{oral}$= 0.3 mg/kg/day; the dermal NOAEL is used to calculate the dermal MOE and the acute oral NOAEL is used to calculate the hand-to-mouth, turfgrass ingestion and incidental soil ingestion MOEs. MOE of 300 is an acceptable margin of exposure.

## Appendix B Acephate Non-Occupational (Recreational) Exposure and Risk Assessment Tables (Short Term Exposures)

**Table 1: Non-Occupational Risk Assessment for Adult Golfers Following Acephate Application to Turf in FL (5.0 lb ai/A -- 2 applications)**

| Day After Treatment | ACEPHATE | | | METHAMIDOPHOS | | |
|---|---|---|---|---|---|---|
| | Average TTR ($\mu g/cm^2$) | Adult Golfer Dose (mg/kg/day) | MOE | Average TTR ($\mu g/cm^2$) | Adult Golfer Dose (mg/kg/day) | MOE |
| 0 | 0.289 | 0.0016 | 7500 | 0.00106 | 0.000006 | 125000 |

NOTE: Values rounded; calculations are based on spreadsheet analyses.

Days After Treatment (DAT). It is assumed that golfers are wearing long pants, long sleeved shirts and no gloves.

Turf Transferable Residue (TTR) averaged from actual field measurements made following the second application.

Adult Golfer Dose (mg/kg/day) = TTR ($\mu g/cm^2$) * Transfer Coefficient (100 $cm^2$/hr for golfing) * (4 hr/day) * (1mg/1000 $\mu g$ conversion factor) ÷70 kg Body Weight. NOTE: this does not include possible hand-to-mouth exposures.

Dermal Short-term MOE = $NOAEL_{dermal}$/ Dose; where $NOAEL_{dermal}$ = 12 mg/kg/day for acephate and $NOAEL_{dermal}$ = 0.75 mg/kg/day for methamidophos. MOE of 100 is acceptable margin of exposure.

**Table 2. Non-Occupational Risk Assessment for 13+ Year-Old Golfers Following Acephate Application to Turf in FL (5.0 lb ai/A -- 2 applications)**

| Day After Treatment | ACEPHATE | | | METHAMIDOPHOS | | |
|---|---|---|---|---|---|---|
| | Average DFR ($\mu g/cm^2$) | 13+ Golfer Dose (mg/kg/day) | MOE | Average DFR ($\mu g/cm^2$) | 13+ Golfer Dose (mg/kg/day) | MOE |
| 0 | 0.289 | 0.0026 | 4620 | 0.00106 | 0.0000096 | 78100 |

NOTE: Values rounded; calculations are based on spreadsheet analyses.

Days After Treatment (DAT). It was assumed that children golfers are wearing long pants, long sleeved shirts and no gloves.

Turf Transferable Residue (TTR) averaged from actual field measurements made following the second application.

13+ Year-Old Golfer Dose (mg/kg/day) = TTR ($\mu g/cm^2$) * Transfer Coefficient (100 $cm^2$/hr for golfing) * (4 hr/day) * (1mg/1000 $\mu g$ conversion factor) ÷44 kg Body Weight. NOTE: this does not include possible hand-to-mouth exposures.

Dermal Short-term MOE = $NOAEL_{dermal}$/ Dose; where $NOAEL_{dermal}$ = 12 mg/kg/day for acephate and $NOAEL_{dermal}$ = 0.75 mg/kg/day for methamidophos. MOE of 100 is acceptable margin of exposure.

## Appendix C Documents Used in the Methamidophos Human Health Risk Assessment

The following memoranda have been incorporated and/or considered in this revised HED Human Health Assessment.

1 Methamidophos - Report of the Hazard Identification Assessment Review Committee, Jess Rowland, Executive Secretary, HED DOC. NO. 012477, 2/12/98.

2 Methamidophos - Revised Product and Residue Chemistry Chapters for the Reregistration Eligibility Decision, Felecia Fort, DPBarcode D259664, 10/1/99.

3 Methamidophos - Revised Toxicology Chapter for RED, Nancy McCarroll, DPBarcode D256737, 7/1/99

4 Methamidophos: Support for the Toxicology Endpoint Selection - For Dermal Risk Assessments - Impact of New Two-Generation Reproduction Study on Dietary and Non-Dietary Assessments, Nancy McCarroll, HED DOC. NO. 013672, 7/28/99

5 Methamidophos -Revisions of the Toxicology Chapter for the RED Document to Include Comments from the Registrant and Other Interested Members of the Public/Formal Response to the Comments Received from the Registrant and Other Interested Members of the Public, Nancy McCarroll, DPBarcode D256737, 7/1/99.

6 Methamidophos - Revised Dietary Exposure and Risk Analyses for the HED Revised Human Health Risk Assessment and HED Review of the Bayer Corporation Probabilistic (Monte Carlo) Acute Dietary Exposure Assessment, F. Fort and Kristina El Attar, DPBarcode D256039, and D256042, 10/4/99.

7 Methamidophos: Revised Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document, Susan Hanley, DPBarcode D258447, 8/9/99.

8 FQPA SAFETY FACTOR RECOMMENDATIONS FOR THE ORGANOPHOSPHATES: A Combined Report of the Hazard Identification Assessment Review Committee and the FQPA Safety Factor Committee, Brenda Tarplee and Jess Rowland, 8/6/98

9 Surface and Groundwater Numbers for the HED Risk Assessment for Methamidophos, Stephanie Syslo, 11/5/98

10 **Acephate.** Revised Human Health Risk Assessment. HED Chapter for the Reregistration Eligibility Decision (RED) Document. List A Reregistration Case 0042. Chemical No. 103301. DP Barcode D259663, Felecia Fort, 10/14/99.